

**HEDONIC PREDICTORS OF TOBACCO DEPENDENCE:
A PUFF GUIDE TO SMOKING CESSATION**

by

Chantal E. Meloscia

Thesis submitted to the Faculty of the
Medical and Clinical Psychology Graduate Program
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Master of Science 2015



UNIFORMED SERVICES UNIVERSITY, SCHOOL OF MEDICINE GRADUATE PROGRAMS
Graduate Education Office (A 1045), 4301 Jones Bridge Road, Bethesda, MD 20814



April 7, 2015

APPROVAL SHEET

Title of Dissertation: **"Hedonic predictors of tobacco dependence: A puff guide to smoking cessation"**

Name of Candidate: Chantal Meloscia, Master of Science in **Medical and Clinical Psychology**,

Date 04/7/2015

THESIS AND ABSTRACT APPROVED:

Dr. Neil E. Grunberg, Ph.D.
DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY
Committee Chairperson

DATE:

4/10/15

Dr. Andrew J. Waters, Ph.D.
DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY
Thesis Advisor

4/10/15

Dr. David S. Krantz, Ph.D.
DEPARTMENT OF MEDICAL AND CLINICAL PSYCHOLOGY
Committee Member

4-8-15

ACKNOWLEDGEMENTS

I would like to acknowledge the United States Navy for allowing me the opportunity to forge my way through three different career fields. After time as a Surface Warfare Officer and Information Warfare Officer, I am thrilled to be embarking on my career as a Navy psychologist.

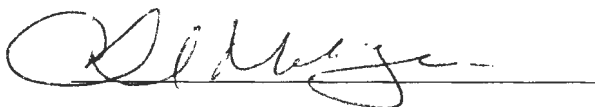
I am forever grateful for the chance to attend the Uniformed Services University of the Health Sciences and thankful for the support I have received from both the Graduate Education Office and the Department of Medical and Clinical Psychology.

My thesis committee has provided invaluable feedback and mentorship for this process and future endeavors. I thank Dr. Neil Grunberg and Dr. David Krantz for their thoughtful editing and words of wisdom.

Finally, I would like to acknowledge my advisor Dr. Andrew Waters. Over the past three and a half years at USUHS, he has expertly guided me along the way to achieving the milestones necessary to achieving success in this program. His ability to mentor with humor, patience, and sincerity is exceptional.

COPYRIGHT STATEMENT

The author hereby certifies that the use of any copyrighted material in the thesis manuscript entitled: Hedonic Predictors of Tobacco Dependence: A Puff Guide to Smoking Cessation is appropriately acknowledged and, beyond brief excerpts, is with the permission of the copyright owner.

A handwritten signature in black ink, appearing to read 'Chantal E. Meloscia', written over a horizontal line.

Chantal E. Meloscia

May 15, 2015

ABSTRACT

Hedonic Predictors of Tobacco Dependence: A Puff Guide to Smoking Cessation

Chantal E. Meloscia, B.A., 2015

Thesis directed by: Andrew J. Waters, Ph.D., Associate Professor, Medical and Clinical
Psychology Department

Cigarette smoking remains the leading preventable cause of death in the United States. Here we examined the clinical relevance of pleasurable effects (“liking”) of cigarette smoking. Smokers (N=268) enrolled in a smoking cessation study were followed from two weeks pre-quit through four weeks post-quit. At each pre-quit session, participants smoked a cigarette. After each of the first seven puffs, they rated puff liking (1-7 scale). After the cigarette, participants also rated their overall liking for the cigarette. Participants who reported higher puff liking ratings were more likely to relapse during the first week (OR = 1.45, 95% CIs = 1.07 - 1.97, $p = .02$). Liking ratings from the most preferred puff (“peak”) were more strongly related to retrospective liking ratings and dependence scores than liking ratings from a random puff. Interventions that attenuate the acute subjective pleasurable effects of cigarette smoking, particularly peak ratings, may facilitate smoking cessation.

TABLE OF CONTENTS

LIST OF TABLES	viii
LIST OF FIGURES	ix
CHAPTER 1: Background.....	1
Smoking Mortality	1
Smoking Morbidity	2
Smoking Prevalence.....	2
Smoking Costs	3
Smoking and the United States Military	3
Smoking Cessation.....	4
CHAPTER 2: Study Background	5
Liking versus Wanting.....	5
Liking Terms.....	6
Liking Mechanisms.....	7
Short Term Liking: Experienced Utility	8
Long Term Liking: Remembered Utility and The Peak End Rule	8
Utility in This Study.....	9
Relapse/Reinforcement	9
Prior Studies.....	11
Contextual Variables.....	12
Study Rationale	13
Study Aims and Hypotheses	14
CHAPTER 3: Methods	16
Participants.....	16
Inclusion and Exclusion Criteria.....	16
Procedure	17
Orientation Measures	18
Fagerström Test of Nicotine Dependence.....	18
Rapid Estimate of Adult Literacy in Medicine	18
Patient Health Questionnaire	18
Mini International Neuropsychiatric Interview	18
Shipley Institute in Living Scale.....	19
Expired Breath CO	19
Study Measures	19
Puff-by-Puff Ratings.....	19
Nicotine Dependence	20
Smoking Diary	20
Biological Measures.....	21

Relapse	22
Analytic Plan	22
Power	25
CHAPTER 4: Results	26
Participant Flow	26
Specific Aim 1	26
Specific aim 2	27
Specific Aim 3	29
CHAPTER 5: Discussion.....	31
Limitations	34
Strengths	35
Implications.....	36
Future Directions – Research Implications.....	37
Appendix A: USUHS IRB Approval	49
Appendix B: MDACC Approval of Data Transfer	50
Appendix C: USUHS Informed Consent Form	51
Appendix D: CO Monitor Instructions	57
APPENDIX E: Self-Report Measures	58
Fagerström Test for Nicotine Dependence	58
Puff-by-Puff Ratings	59
Overall Cigarette Ratings.....	60
Smoking Diary	61

LIST OF TABLES

Table 1. Participant Demographics and Smoking Characteristics.....	39
Table 2. Summary Statistics for Liking Ratings.....	40
Table 3. Correlations between Puff Liking Ratings and FTND scores in the Abstinent and Non-abstinent visits.	41

LIST OF FIGURES

Figure 1. Overall graphic of wanting and liking processes involved in the progression to smoking relapse.	42
Figure 2. Study design.	43
Figure 3. Puff Liking Ratings (1-7 scale) by Puff Number and Abstinence State (N = 227).	44
Figure 4. Puff Liking Ratings (1-7 Scale) by Week +1 Relapse status, Puff Number and....	45
Abstinence State (ns = 166 relapsers, 33 abstainers (non-abstinent); 162 relapsers, 31 abstainer (abstinent state).....	45
Figure 5. Mean retrospective ratings with Puff Liking Ratings (1-7 scale) by Puff Number and Abstinence State (N = 227).	46
Figure 6. Peak-end analysis for retrospective ratings of cigarette liking.....	47
Figure 7. Peak-end analysis for FTND.	48

CHAPTER 1: Background

SMOKING MORTALITY

Cigarette smoking is related to several life threatening diseases including lung cancer, coronary heart disease, and stroke. Further, smoking is the leading preventable cause of death with cigarette smoking being linked to approximately 480,000 deaths in the United States each year. Long-term smoking can also decrease life expectancy by about ten years. General life expectancy for men and women in the United States in 2009 was 76 years and 81 years, respectively. Life expectancy with smoking for men and women was 66 years and 71 years, respectively (48).

Smoking is a risk factor for many of the top ten causes of death in the US including heart disease, cancer, and chronic lower respiratory diseases (the top three leading causes of death in the United States in 2010). Specifically, for heart disease, men who smoke increase the risk of dying from heart disease by four times and women by five times. Men who smoke increase the risk of dying from lung cancer by twenty-three times and women by twelve times. Regarding chronic lower respiratory diseases, men who smoke increase their risk of dying from respiratory disease by seventeen times and women by twelve times (6).

Overall, medical research suggests that smoking can greatly increase the chance of death. In fact, the Surgeon General's most recent report on smoking, *The Health Consequences of Smoking – 50 Years of Progress*, states that cigarette smoking causes about one of every five deaths in the United States each year (48).

SMOKING MORBIDITY

Besides contributing to mortality, there are many detrimental health effects associated with smoking including reduced fertility, reduced bone density, tooth loss, and arthritis. Further, smoking leads to overall increased inflammation in the body causing reduced immune functionality. Additional health issues include increased risk for stroke and coronary heart disease (6). The recent Surgeon General's report on smoking reports that more than 16 million Americans suffer from a disease caused by smoking (48).

SMOKING PREVALENCE

Despite the known health risks and economic costs associated with smoking, the prevalence of smoking for adults (18 years of age and older) in the United States in 2012 was about 18%; smoking was defined as a person who currently smokes every day or most days and has smoked greater than or equal to 100 cigarettes in their lifetime. Further, declines in cigarette smoking have been minimal over a recent 5-year period (2005-2010) with only about a 1.5% decrease (6).

Looking at trends in smoking prevalence over the past 35 years, it is evident that the number of smokers in the United States is not decreasing. A review by the CDC of the number of smokers each year from 1974-2009 showed that while there was a slight decrease in the number of smokers from the 1970's to the 1990's, since then rates have remained steady with women smoking slightly less than men (7).

Also, globally smoking prevalence has been increasing. A recent study (25) states that "The number of smokers has increased steadily worldwide, and there are preliminary indications that global prevalence among men increased in recent years" (p.183). Despite increased

awareness (24) of the risk of smoking for mortality and morbidity, smoking prevalence in the United States and around the world is either remaining steady or increasing.

SMOKING COSTS

When reviewing the negative impacts of smoking, the costs associated with smoking-related illness and death is important to consider because costs affect communities and societies. The estimated economic burden for health care and loss of productivity in the United States associated with smoking totals about \$289 billion annually, \$133 in medical care costs and \$156 in productivity loss. Further, second hand smoke has been implicated in non-smoker deaths from lung cancer, about 7,300 deaths annually, and heart disease, about 34,000 deaths annually (48).

SMOKING AND THE UNITED STATES MILITARY

Given the number of United States' citizens that serve in the United States military and the health and economic impact of smoking, it is important to consider the prevalence of smoking in this specific population. The United States military has an overall smoking prevalence of 24% across all branches of service (8% greater than the prevalence in the general United States population). Further, 3.2% of the military population identify as heavy smokers (11). Productivity loss for the active duty military has been estimated at 346 million dollars (4).

Beyond the financial cost of smoking for the military, an Institute of Medicine (IOM) report from 2009 summarizes possible operational costs associated with smoking. Smoking service members can have lower visual acuity and reduced night vision compared to non-smoking service members. The IOM report also reported additional adverse health effects of tobacco use for the military population including decreased cognitive ability and impaired respiratory function that affect aviation performance and military driving. Also, smoking service members are more likely to develop musculoskeletal injuries than their non-smoking

counterparts (19). Finally, smoking is known to decrease the ability for wounds to heal efficiently. The nicotine and carbon monoxide in cigarettes interfere with the normal wound healing process (42). This effect is crucial to consider in the military combat environment.

The research shows that smoking is not only detrimental to an individual service member's health and productivity, but also to a military unit's ability to function. For example, decreased cognitive ability would increase the chances for a pilot landing on an aircraft carrier to miss his/her landing and crash on the deck of the carrier. Taking the time to rescue the crew and clear the crash could mean life or death for ground troops waiting for timely air support (19).

SMOKING CESSATION

Given the associated health risks and other negative aspects of smoking cigarettes (cost, smell, etc.), most smokers are motivated to quit; however cessation is difficult. The majority of quit attempts end in relapse within four weeks (51). Nicotine replacement therapy that targets biological aspects of the addiction is an effective treatment (41), however relapse is still common (51). Other medications that have been reported as effective in helping people quit smoking include varenicline and bupropion (18). Despite access to pharmacotherapies such as nicotine replacement therapy, varenicline, and bupropion, most smokers still attempt to quit without using pharmacotherapy (8). Additionally, some behavioral and cognitive treatments have been effective, but again relapse among those treated is common (15). Current research is continuing to explore the effectiveness of cognitive and behavioral treatments as well as treatment combinations that include both medication and a cognitive and/or behavioral intervention (for example, 3, 13). In sum, while many different methods of smoking cessation treatment show a level of efficacy, relapse rates in all studies are still high.

CHAPTER 2: Study Background

As discussed in the previous chapter, smoking is prevalent, a leading cause of death, and a financial burden on society. Despite many smokers reporting that they are motivated to quit smoking, relapse after smoking cessation is common and current behavioral treatments and pharmacotherapies have only limited success aiding people to quit smoking. To develop more effective interventions, a deeper understanding of the psychological processes underlying relapse to smoking is necessary. The current study explored the psychological process of the acute “liking” effects of smoking. Figure 1 guides the framework of this chapter beginning with the overarching umbrella of subjective experience through smoking relapse/use. As seen in Figure 1, subjective experience is the broad category for the processes relevant to understanding the background to this study. “Subjective experience” has been connected with broad topics such as mood, but also encompasses more specific ideas such as alertness or tension (21). Two of the major categories of subjective experience are “liking” and “wanting”. In the literature, the processes of wanting and liking (see Figure 1) have been investigated as separate pathways to smoking relapse.

LIKING VERSUS WANTING

Prominent researchers have suggested that there is a distinction between drug “wanting” and drug “liking.” “Wanting” has been described as “the underlying core process that instigates goal-directed behavior, attraction to an attention stimulus, and consumption of a goal object,” and liking is “the underlying core process of hedonic evaluation that typically produces conscious pleasure” (2). More specifically, Robinson and Berridge (34) suggested that the neural system responsible for drug “wanting” is independent of the neural system associated with drug “liking.” Reviewing the literature regarding the role of dopamine in reward, Berridge and

Robinson (2) explain their incentive salience hypothesis by suggesting that dopamine mediates the neural pathway for “wanting,” but that there is a separate neural pathway for “liking.” Based on studies assessing “liking” and “wanting” associated with dopamine deprived rats, Berridge and Robinson (2) discuss that dopamine-depleted rats are still able to “like” rewards (such as sugar water), but that these rats do not “want” the reward. (In these rat studies, to explore the difference between “liking” and “wanting,” researchers used measures such as consumption and quantity preference for “wanting” and measures of taste reactivity for “liking.” Please see Robinson and Berridge (34) for detailed information on measures.) Therefore, liking and wanting can be considered as two separable processes involved in nicotine addiction that warrant individual study (2).

Much research on psychological processes of smoking has focused on drug “wanting” with indices of wanting including variables such as craving, approach behavior, and attentional bias (34). For example, Kozlowski and Wilkinson (22) discussed that there may be differences between the meaning of “urge” versus “craving” in regards to drug addiction. Ten years later, Shiffman et al. (36) reported that in their research they found that the two measures of craving and urges were highly correlated based on self-report from participants trying to quit smoking. A review of the literature shows that the indices of varying psychological processes of smoking continue to be investigated as these indices are likely to have a crucial role in understanding how to aid with smoking cessation. Another psychological process that is important to address is subjective smoking satisfaction, or drug “liking.” Individual differences in cigarette smoking liking may be related to nicotine dependence and relapse.

LIKING TERMS

Many terms are used in the drug “liking” literature to assess the processes that are hypothesized to be occurring. The terms “satisfaction” and “pleasure” have been used in smoking studies as a measure of self-reported liking. Prior studies have found no significant difference in correlational results when asking about the subjective pleasure or satisfaction of a cigarette. Specifically, pleasure and satisfaction were highly correlated and exhibited a similar pattern of relationships with study variables (39). Other studies have used the word “liking” to investigate the effect of the subjective experience. For example, in Perkins et al. (28), the question used during the procedures was the word “liking.” The assumption is that the results from asking about liking, satisfaction, and pleasure are very similar, as suggested by Shiffman and Kirchner (39). That is, no major theoretical or empirical differences have been hypothesized or observed between the terms liking, satisfaction, and pleasure.

LIKING MECHANISMS

Historically, addiction had thought to be mediated by subjective liking. At the most basic level, all addictive drugs elicit pleasure, and subjective drug effects may be reinforcing (46). Further, memories of past pleasure might mediate addiction (34), so that both the actual smoking experience and recall of that smoking experience may play a role in relapse. Shiffman and Kirchner (39) described this idea in their recent study: “More satisfied smokers might have greater difficulty quitting and staying quit because they value and miss cigarettes more” (p. 2). They suggested that subjective ratings of smoking could be valuable to understand the pattern that leads to relapse. For example, the first cigarette smoked may be a trigger for relapse for those who subjectively rate smoking as more pleasurable and such individuals will be more likely to progress to full relapse after an initial lapse (39).

When investigating the effects of liking on smoking relapse and dependence, examining the differences between short-term ratings of liking and long-term ratings of liking after smoking may be important to understand the pattern of relapse and dependence. Figure 1 depicts these two temporal ideas showing the concepts associated with short-term liking and long-term liking.

SHORT TERM LIKING: EXPERIENCED UTILITY

The two concepts being considered for short-term liking in this study are acute hedonic effects and experienced utility. Hedonic is a term that encompasses the category of subjective pleasure responses to smoking. Liking, satisfaction, and pleasure are in the category of hedonic response to smoking. Acute pertains to the short-term response after smoking a cigarette or even after one puff (as examined in this study). Therefore, acute hedonic effects refer to the short-term pleasurable effects of smoking. Subjective hedonic responses can be considered potent reinforcers. Smokers who experience more subjective pleasure and satisfaction are more likely to continue smoking (37). The second concept included in the conceptualization of short-term liking is Kahneman's (20) idea of "experienced utility." He defines experienced utility as the moment-to-moment flow of pleasure or pain; the way people feel about experience in real time. Measuring the acute hedonic effects of smoking allows for assessment of a smoker's experienced utility.

LONG TERM LIKING: REMEMBERED UTILITY AND THE PEAK END RULE

In addition to the short term, "in the moment," ratings of subjective liking during smoking, research suggests that longer-term memories of smoking could be an important factor in smoking relapse. Kahneman (20) described a phenomenon known as "remembered utility"; the way people remember the experience after it is over. Also, Kahneman (20) formulated a heuristic for remembering pleasure known as the "peak end rule." (Heuristics are experienced

based techniques for problem solving, learning, etc. that are efficient but are not guaranteed to be optimal). The peak end rule is the concept that retrospective evaluations of affective episodes are more influenced by affective experience at two moments, the most extreme moment and the end moment. For example, the perceived best day (most pleasurable) and the last day on a vacation will be better predictors of remembered enjoyment than the average pleasure rating (aggregated across days) or the pleasure of a day selected at random. For this study, measuring the remembered utility and assessing for the peak end rule in regards to “liking” allowed for a comparison to experienced utility. Further, confirmation that the peak end rule functions for cigarette liking provided a framework for novel clinical interventions.

UTILITY IN THIS STUDY

One main purpose of this study was to examine the subjective pleasure experienced during each puff of a cigarette (experienced utility of acute hedonic effects) versus the remembered utility of a whole cigarette. Participants were asked to rate smoking pleasure after each puff (experienced utility) of a cigarette smoked as usual. They were then asked to rate the overall pleasure after smoking seven puffs of the cigarette (remembered utility).

RELAPSE/REINFORCEMENT

Finally, the term “reinforcement” must be considered in the context of cigarette “liking.” A reinforcer is a stimulus that is likely to increase the frequency of a behavior. In human laboratory studies, smoking reinforcement can be measured by asking a person to choose to intake nicotine or not (such as smoke a cigarette or not). For example, Henningfield and Goldberg (17) used a self-administration paradigm of intravenous nicotine to explore self-administration based on positive and negative reinforcement. Further, some studies include the amount of smoking that a participant does as a measure of reinforcement. For example, Perkins

et al. (29) defined smoking reinforcement, a dependent variable in their study, as the latency to first puff and the total number of puffs taken.

Intuitively one might think that subjective sensations, such as the pleasurable effects of smoking, are always linked to (or cause) reinforcement. That is, one might think that it is the pleasurable effects of smoking that reinforce the behavior (increase smoking). However, this process may not always be the case. While Perkins et al. (31) showed the potential for a connection between puff volume, considered reinforcement, and liking ratings, there is also evidence to suggest that individuals will self-administer in the absence of pleasurable effects. Most importantly, Robinson and Berridge (34) suggest that the pleasurable effects cannot always explain drug reinforcement. They suggest that as a person uses an addictive drug, the brain becomes sensitized to the drug and results in an increase in “incentive salience” towards that drug and drug-related cues. Even if someone does not like a drug, his or her brain may still crave (want) the drug based on brain neuroadaptations. Additionally, some cocaine studies have shown reinforcement behavior (increased self-administration of low doses of cocaine) in the absence of any pleasure (see 34). The incentive salience hypothesis of drug addiction posits that there are three contributors to addiction: “liking,” “wanting,” and learning (1).

Although subjective ratings of hedonic responses do not necessarily always drive behavior, research does suggest that there is a connection between subjective responses to smoking and reinforcement (46). However, Kalman (21) indicates that the connection between the subjective experience of cigarette smoking and the reinforcing value of the nicotine in cigarettes has not been well characterized. The present study adds to the research examining the connection between subjective liking of smoking, both in the moment (short-term) and remembered (long-term), and smoking relapse.

PRIOR STUDIES

Two recent studies, including one laboratory study and one Ecological Momentary Assessment (EMA) study, provide useful data on the acute hedonic effects of smoking for the current study. Shiffman and Kirchner (39) measured smoking satisfaction ratings in 394 heavy smokers on a cigarette-by-cigarette basis on palm top computers for 16 days of ad libitum smoking prior to a quit day. They measured satisfaction and pleasure ratings separately, but analyzed the two measures together based on lack of difference between them. Heavy smokers with greater average ratings of satisfaction after smoking had a higher rate of relapse in a subsequent quit attempt. The effect was not due to nicotine dependence (assessed using the Fagerström Test of Nicotine Dependence), suggesting that memory of how satisfying smoking was may promote relapse (39).

In 2012, Perkins and colleagues investigated the reliability of subjective ratings after participants (dependent smokers) smoked one cigarette in the lab. After smoking as usual before each lab visit, participants were asked to smoke one cigarette of their preferred brand in the lab ad libitum. After finishing the cigarette, participants were asked to rate subjective responses to two questions: “How much do you like the puffs you just took?” and “How strong was that cigarette?” Perkins et al. (28) reported “subjective measures during the ad lib smoking of a single cigarette are highly reliable” (p. 490) and concluded that this measure could be useful for future studies attempting to measure individual differences in subjective ratings of smoking. The study also found that liking ratings were higher for smokers with higher nicotine dependence (28).

CONTEXTUAL VARIABLES

Certain contextual variables might moderate liking ratings of puffs. Factors such as eating, drinking alcohol, drinking beverages with caffeine, and smoking with other smokers can change an individual's pattern of smoking (38) and may influence liking ratings. One prominent variable that is expected to moderate liking is the level of nicotine deprivation.

Nicotine has been identified as the main component of tobacco that causes addiction. Nicotine is a chemical that is absorbed into the bloodstream and passes through the blood-brain barrier into the brain. During regular use of cigarettes, nicotine is present in the body at all times, and smokers develop tolerance to nicotine. Nicotine produces pleasurable effects, but adaptations to nicotine cause negative withdrawal symptoms during nicotine deprivation for most people (47). Because nicotine produces pleasurable effects, and because abstinence from nicotine is unpleasant, it is useful to explore the subjective effects of smoking while a smoker has been smoking as usual as well as during short-term abstinence from smoking to obtain a more comprehensive picture of the acute subjective effects of nicotine.

Smokers report that the initial cigarette of the day, following a period of deprivation, often provides the largest rating of pleasure and that the following cigarettes produce less of an effect of pleasure (32). This effect can be attributed to the effects of "acute tolerance" (31). Nicotine is thought to acutely desensitize nicotinic receptors ("acute tolerance") and so the drug effect should be strongest when there is less receptor occupation. The same phenomenon might be relevant across puffs. Another complicating factor with deprivation state is that abstinence from smoking itself causes increases in negative affect (e.g., 39), and so smoking may be reinforcing due to its ability to ameliorate the aversive state of abstinence ("negative reinforcement"). In other words, smoking when abstinent may be pleasurable not only because of the absence of acute tolerance to the effects of nicotine, but also due to the fact that it may

rapidly ameliorate abstinence symptoms. Finally, deprivation can affect other variables in an individual that may affect within-subject liking ratings. For example, Cinciripini and colleagues (9) studied the effects of smoking deprivation on emotion and found that deprivation can cause within-subject differences on variables such as salience to smoking stimuli and response to negative emotional stimuli. They reported that smoking stimuli salience and response to negative emotional stimuli both increased during a short period (12 hours) of smoking abstinence (9).

STUDY RATIONALE

For this study, the strengths from the two previous studies described were built upon. Shiffman and Kirchner's (39) study had people who were trying to quit and Perkins et al. (28) study was the first to assess "liking ratings" in a lab setting. This study was the first to assess puff-by-puff liking in the lab for smokers who are motivated to quit smoking. The format of the study was a prospective cohort smoking cessation study that examined the association between hedonic effects assessed in the lab and smoking dependence and relapse. The study provided an improved understanding of hedonic effects, which can inform smoking cessation efforts.

In this study, participants were asked to take seven puffs of their preferred cigarette brand while in the lab. After each puff, participants entered liking ratings on a lab computer. These data provided a measure of experienced utility (in the moment smoking satisfaction). This puff-by-puff measure allowed for the examination of the association of liking ratings for different puff number with relapse and dependence.

Puff-by-puff ratings were taken on two occasions, once when participants were overnight abstinent from smoking, and once when participants had been smoking normally. As noted earlier, for a given dose of nicotine, subjective effects are stronger when participants are

abstinent (e.g., 31). Therefore, it was expected that liking effects would be greater at earlier puffs and when participants were abstinent.

After participants smoked the cigarette in the lab, they were asked to rate the overall pleasure of smoking the cigarette. This measure of remembered utility allows for a comparison of remembered utility versus experienced utility and the peak end rule in the context of smoking.

STUDY AIMS AND HYPOTHESES

Specific Aim 1: To describe puff-by-puff liking ratings in the laboratory of cigarette smokers preparing for a quit attempt.

Hypothesis 1.1: Participants will differ in their liking ratings of each puff of a cigarette.

Hypothesis 1.2: Participants' liking ratings will decline over seven puffs of a cigarette.

Hypothesis 1.3: Puff-by-puff liking ratings will be higher when participants are measured in the abstinent state versus the non-abstinent state.

Specific Aim 2: To examine the clinical relevance of acute hedonic effects ("liking") of smoking.

Hypothesis 2.1: Participants who report greater hedonic effects (liking) from smoking will have higher Fagerström Test of Nicotine Dependence (FTND) scores.

Hypothesis 2.2: Participants who report greater hedonic effects (liking) from smoking are more likely to relapse to smoking after a quit attempt.

Specific Aim 3: To explore the relationships between experienced and remembered utility of smoking and the relationship of these two forms of utility with dependence.

Hypothesis 3.1: To explore whether Peak (highest rated puff) liking and End (last puff) liking will predict retrospective liking ratings better than liking from a puff selected at random.

Hypothesis 3.2: To explore whether Peak (highest rated puff) liking and End (last puff) liking will predict FTND scores better than liking from a puff selected at random.

CHAPTER 3: Methods

PARTICIPANTS

This study was a secondary analysis of data (N=268) collected in a multi-site smoking cessation study at the University of Texas M. D. Anderson Cancer Center in Houston, Texas (n=150), and at the Uniformed Services University of the Health Sciences in Bethesda, MD (n=118). The parent study included participants who were attempting to quit smoking without the use of pharmacotherapy. Brief individualized counseling, both in person and over the telephone, was given.

Overall, 268 participants, who met the study pre-screening requirements, attended an orientation session and signed the informed consent form. The Institutional Review Board (IRB) of each institution approved the consent form. An example of the USUHS consent form is included in Appendix C. Of the 268 participants, 237 participants provided puff-liking ratings on at least one session. Participant attendance declined over the six laboratory sessions of the study. Participant demographics and smoking information for these participants are shown in Table 1. On average, participants were moderate to heavy smokers with mean cigarettes smoked per day of approximately 20 cigarettes per day. The mean FTND score was 5.15, indicating moderate nicotine dependence.

INCLUSION AND EXCLUSION CRITERIA

Prior to reporting for the orientation session, participants were screened via telephone. If they were eligible after phone screening, then participants were given the option to schedule an orientation session in the laboratory where they were screened further before being admitted to the study. There were several inclusion criteria for the study. Participants had to be current

smokers between the ages of 18 and 65 who smoked at least 10 cigarettes per day for the last year and were motivated to quit smoking. Also, participants had to have a home address, functioning telephone number, and 8th grade reading/writing/literacy level in English (assessed using a literacy test described below).

Exclusion criteria included regular use of tobacco products other than cigarettes (cigars, chewing tobacco, etc.), use of nicotine replacement therapy (NRT), and use of other smoking cessation medications (such as Varenicline and bupropion). These criteria were assessed using self-report to the research assistant conducting the phone screening. Additional exclusion criteria included an expired breath carbon monoxide (CO) level less than 10 parts per million (ppm) (this measure ensures regular cigarette use), serious mental illness (major depression or active suicide ideation), current substance abuse, and/or having another household member enrolled in the study.

PROCEDURE

The study protocol included six laboratory visits. Sessions consisted of an orientation session, two pre-quit sessions (Week -2 and Week -1), the quit day visit, a visit one week after the quit day (Week +1), and a visit at the end of treatment (four weeks after quit day) (Week +4). For the two pre-quit sessions, participants attended once when 12-hours abstinent from smoking and once when smoking normally. These sessions were counterbalanced. A figure illustrating the study procedures is included (see Figure 2). Some participants ($n = 119$) provided data from participating in a 1-week Ecological Momentary Assessment (EMA) study which started on quit day (see 48).

Orientation Measures

During the orientation session, participants were given several measures to assess for inclusion and exclusion criteria.

Fagerström Test of Nicotine Dependence

The Fagerström Test of Nicotine Dependence (FTND) (16) was used to measure nicotine dependence. The FTND has a Cronbach's alpha of .64 and was tested to be reliable and valid (32).

Rapid Estimate of Adult Literacy in Medicine

The Rapid Estimate of Adult Literacy in Medicine (REALM) was used as a literacy screener. An 8th grade reading level as assessed by this measure was required for inclusion in the study. The REALM is a well-validated measure for assessing literacy level in primary care and public health settings. When REALM results were correlated with three other standardized reading tests, the REALM results were all significant (10).

Patient Health Questionnaire

The Patient Health Questionnaire (PHQ) was administered to assess for depressive and suicidal symptomology. This questionnaire includes nine items that follow the DSM-IV criteria for depression. The PHQ has been researched and found to be reliable and valid (23).

Mini International Neuropsychiatric Interview

The Mini International Neuropsychiatric Interview (MINI) was used to assess for non-alcohol substance use, an exclusion criteria for the study. The MINI has been found to be a reliable and valid measure (35).

Shipley Institute in Living Scale

The Shipley Institute in Living Scale (Shipley) was administered to evaluate intellectual ability. The Shipley has been found to be a reliable measure of intellectual ability with results correlating significantly with college student grade point averages (26).

Expired Breath CO

Smoking status was biochemically verified using expired breath CO with a portable CO monitor in the lab during the orientation session and at all other lab sessions (explained in detail in the “Measures” section below).

Study Measures

Particularly pertinent for this study were ratings of puff-by-puff liking at the two pre-quit sessions (one where smokers had remained abstinent for 12 hours prior and one where smokers had smoked regularly prior to the session). These sessions were counterbalanced across participants, so that half the participants (odd-numbered participants) completed the non-abstinent session first and the other half (even-numbered participants) completed the abstinent session first. If a participant reported smoking on the day of the abstinent session or had high CO levels (> 10 ppm) then their abstinent visit was rescheduled.

Puff-by-Puff Ratings

Participants smoked a cigarette (their preferred brand) at each of two sessions prior to quit day in the lab’s “Smoking Lab.” Participants were asked during the initial phone screening what their preferred brand of cigarette was and whether their regular brand was menthol or non-menthol; 53% reported smoking non-menthol cigarettes and 47% smoking menthol cigarettes.

Participants reported smoking many brands of cigarettes with the most frequent being Marlboro (33%) and Newport (23%).

For the ratings, participants were asked to smoke seven puffs of one cigarette as they would usually. After each puff, participants were asked to enter a “liking” rating after each puff (experienced utility) on a computer in the lab. At the end of smoking the cigarette, they were asked to enter their overall liking rating (remembered utility) on the lab computer. A research assistant observed from outside of the room to ensure compliance.

The item that participants answered after smoking each puff was “How much did you like the last puff?” The question was on a scale of 1-7 with the anchor at number 1 of “Didn’t like at all” and the anchor at number 7 of “Liked it very much.” The item administered after the cigarette was “Overall, how much did you like the last cigarette?” which had the same 1-7 scale and anchors as the post-puff item.

Nicotine Dependence

The FTND is a six-item self-report questionnaire that is used to assess nicotine dependence severity, and has been used in a large number of studies (16). This measure is described more fully in an earlier section.

Smoking Diary

The smoking diary is a paper form containing boxes for each study day (Appendix F). Participants were instructed to make an entry each day at bedtime indicating how many cigarettes they had smoked that day. Smoking diaries, both paper and electronic, have been used in many smoking studies. For example, Brown and colleagues (5) used a smoking diary to validate the timeline follow back method, a retrospective assessment of smoking patterns. The smoking diary is a simple method to gather self-reported number of cigarettes smoked daily.

Biological Measures

Carbon monoxide (CO) monitors (Bedfont Micro Smokerlyzer, Harrietsham, England) were used to assess participants' CO expired breath levels at each lab session. The participants followed the manufacturer's instructions (Appendix D) when using the device. The CO monitors were regularly calibrated using a cylinder of research gas with a known CO concentration. CO measurements are used to assess recent smoking (in the last 48 hours). CO level is related to the uptake of nicotine in the blood stream, and the CO monitor provides an indirect measure of this. CO expired breath levels are often used to validate self-reported smoking abstinence (45). CO level was used to assess if a participant was abstinent for the abstinent visit session; a breath CO level of less than or equal to 10 parts per million (ppm) was required to be considered abstinent for that visit. Expired CO levels below 10 ppm are considered an indication of no smoking or very light smoking (45).

Salivary cotinine, a major metabolite of nicotine, has been described as the "gold standard" for measuring nicotine exposure (27). A more recent review of studies using cotinine as a measure of confirming self-reported smoking status reported that cotinine is a more accurate measure of smoking status compared to self-report (14). Participants were asked to place a small cotton swab in their mouth for one minute. The participant then placed the swab in a test tube without using his or her hands. The test tube was labeled and then placed in a centrifuge to extract the saliva. The sample was frozen before being shipped to Salimetrics LLC (State College, PA) (a company that performs biological assays) for the cotinine assay. Salivary cotinine levels were measured through an enzyme immunoassay conducted by Salimetrics.

Relapse

To assess relapse post quit day, data were drawn from three sources: self-reported smoking, expired breath CO, and cotinine in saliva. At the two post-quit sessions (Week +1 and Week +4), relapse was defined as “any smoking, even a puff, during the past 7 days.” Reports of abstinence were biochemically confirmed using carbon monoxide levels in breath and cotinine levels in saliva as described below.

To be considered abstinent at Week +1, participants had to report no smoking on the smoking diary during Week 1, report no smoking on a PDA between quit day and Week +1 (if applicable), have expired breath CO level less than or equal to 10 ppm at Week +1, and have a cotinine level less than or equal to 15 nanograms per milliliter at Week +1. At Week +1, 33 participants out of the 200 participants who attended quit day (16.50%) were coded as “abstinent” using these criteria; all other participants, including those who dropped out of the study, were coded as “relapsed.” To be considered abstinent at Week +4, participants had to report no smoking on the smoking diary during the seven days prior to the Week +4 visit, have expired breath CO level less than or equal to 10 ppm at Week +4, and have a cotinine level less than or equal to 15 nanograms per milliliter at Week +4. At Week +4, 38 out of 200 participants (19.00%) were coded as abstinent using these criteria; all others were coded as relapsed.

ANALYTIC PLAN

For Hypothesis 1.1, descriptive statistics of liking ratings were computed. An intraclass correlation coefficient (ICC) was also computed for the non-abstinent and abstinent state separately using SAS PROC MIXED. The ICC can vary between 0 and 1. If the ICC were 0, then this result would indicate that all subjects would have the same mean puff liking ratings, and therefore, that all of the variability in the data is due to differences in liking ratings across

puffs. As the ICC gets closer to 1, more of the variability in the data is due to the differences between subjects (i.e., participants have different mean liking ratings).

For Hypothesis 1.2, a repeated-measures analysis of variance (ANOVA) with two within-subject variables using SAS PROC GLM was used to examine whether liking ratings changed over puffs. Puff Number was one within-subject variable with 7 levels (Puff Number 1, Puff Number 2, Puff Number 3, Puff Number 4, Puff Number 5, Puff Number 6, Puff Number 7), and Abstinence State was the second within-subject variable with 2 levels (Non-abstinent, Abstinent). A main effect of Puff Number would indicate that liking ratings changed over time.

For Hypothesis 1.3, the repeated-measures ANOVA described for Hypothesis 2.1 was also used to examine the effect of Abstinent State on liking ratings. A main effect of Abstinence State would indicate that liking ratings differed across the two states.

For Hypothesis 2.1, Pearson's Correlation Coefficient was used to examine the correlation between liking ratings and FTND scores. Analyses were examined separately for the abstinent and non-abstinent states and for different puff numbers. To examine whether the associations between liking ratings and FTND scores was moderated by Abstinence State or Puff Number we used the general linear model described in hypothesis 2.1 and added FTND as a continuous independent variable. A significant FTND by Puff Number interaction would indicate that the association between FTND and liking ratings differed across puff numbers. A significant FTND by Abstinence State interaction would indicate that the association between FTND and liking ratings differed across states.

For Hypothesis 2.2, a mixed analysis of covariance (ANCOVA) was used to examine if participants who get greater hedonic effects from smoking were more likely to relapse to smoking in a subsequent quit attempt. The between-subjects independent variable was Relapse

Status at Week 1, with 2 levels (Relapsed, Abstinent). As with Hypothesis 2.1, there were two within-subject variables, Puff Number (7 levels) and Abstinence State (2 levels). The dependent variable was “liking” rating. The covariates were FTND score (continuous) and Order of completion of abstinent and non-abstinent sessions, (2 levels: Non-abstinent first vs. Abstinent first) (“Order”). A second ANCOVA was conducted using Week 4 relapse status as an independent variable.

Logistic regression was also used to confirm the results of the ANCOVA. In this analysis the independent variable was the mean liking rating across puffs, and the dependent variable was relapse status at 1 week. As before, the model included two covariates, FTND score and Order. A second logistic regression was conducted using Week 4 relapse status as the dependent variable.

For Hypothesis 3.1, a series of linear regression analyses were run using SAS PROC REG in which peak liking and end (last puff) liking and “random” puff “liking” were entered simultaneously as predictor variables (i.e., three predictor variables in total), and retrospective liking rating was the dependent variable. The “random” puff rating was a rating from a puff selected at random for each participant by a program written in SAS (using the “ranuni” routine). Because the program selected a different puff each time it was run, different regression coefficients for all three predictor variables would be generated for each linear regression. Therefore, we ran 20 regressions, and took an average of the regression coefficient for each of the three predictor variables (peak liking, end liking, random liking); 95% Confidence Intervals were also calculated. Separate regression analyses were conducted for data in the non-abstinent and abstinent states.

For Hypothesis 3.2, the analytic method was the same as that used for hypothesis 3.1 except that the dependent variable was FTND scores. Again, for both of these hypotheses, data were analyzed separately for the abstinent and non-abstinent states at visits 2 and 3.

POWER

Power analyses were computed using G*Power 3.1.2. Power estimates for 2-tailed tests were set at alpha level of .05. For hypotheses 1.2 and 1.3, which examined between-state and between-puff differences, a sample size of 205 (the number of participants who contributed data in both states) provided power = .81 to detect an effect size, d , in the population of 0.20. For hypothesis 2.1, a sample size of 215 (the number of participants who provided data in the abstinent state) provided power = .80 to detect a population correlation, ρ , of .19. Power was greater for the non-abstinent state, where 227 participants provided data. For hypothesis 2.2, a sample size of 200 (the number of participants who attempted to quit) has power = .80 to detect an Odds Ratio of 1.71 for an independent variable with $M = 0$ and $SD = 0$, assuming a relapse rate of 85% and a sample size of 200. Given that Specific Aim 3 was exploratory in nature, power analyses were not conducted for hypotheses 3.1 and 3.2.

CHAPTER 4: Results

PARTICIPANT FLOW

As noted earlier, 268 participants attended the orientation session, of whom 200 attended quit day and made a quit attempt. Of the 268 participants, 227 participants provided puff data at the non-abstinent session and 215 provided puff data at the abstinent session; as noted above, 237 provided data at least one session, and 205 participants provided puff data at both the non-abstinent and abstinent sessions. Of the 200 participants who attempted to quit, 199 provided puff data at the non-abstinent session and 193 provided puff data at the abstinent session. Data were missing due to equipment or researcher error. A mean puff rating (average of ratings at non-abstinent and abstinent sessions) and relapse data were available for all 200 participants. Table 2 shows summary statistics for liking ratings over all participants.

SPECIFIC AIM 1

Hypothesis 1.1: The ICC was calculated to evaluate if participants differed in their liking ratings. The observed ICCs were 0.75 (hypothesis test vs. 0, $z = 10.1$, $p < .0001$) for the non-abstinent session and 0.66 (hypothesis test vs. 0, $z = 9.6$, $p < .0001$) for the abstinent session. These ICCs are significantly different from 0 meaning that there is significant variability in participant mean liking ratings. Based on this result, the next step is examination of correlations between mean puff ratings and dependence (and relapse). However, there is still some variability that is due to differences between puffs. This result motivates examination of between-puff differences.

Hypothesis 1.2: Puff-liking ratings were generally high, with an average of 5 to 6 on the 7-point scale (Figure 1). Using a repeated measures ANOVA on data with the 205 participants with data at both sessions, liking ratings declined over puffs, as revealed by a significant main

effect of Puff Number, $F(6, 1224) = 92.17, p < .0001$ (higher liking ratings for earlier puff compared to later puffs). Polynomial contrasts revealed a strong linear effect, $F(1, 204) = 140.72, p < .0001$) but no quadratic effect, $F(1, 204) = 0.31, p = .57$, suggesting that puff liking ratings declined gradually in a linear fashion over time through the seven puffs.

Hypothesis 1.3: The repeated-measures ANOVA yielded a main effect of Abstinence State, $F(1, 204) = 4.26, p = .04$. Over all puffs, puff-liking ratings were higher at the abstinent session (mean rating = 5.26) than the non-abstinent session (mean rating = 5.00). This conclusion is qualified by the presence of a significant Puff Number by Abstinence State interaction, $F(6, 1224) = 3.91, p = .0058$. Figure 3 reveals that puff liking ratings were higher at the abstinent (vs. non-abstinent) session at early but not later puffs (Figure 1). Pairwise comparisons were calculated (unadjusted) and showed a significant effect of state at puffs 1 ($p = .003$), 2 ($p = .0007$) and 3 ($p = .005$), but not at later puffs (all $ps > .22$). Therefore, abstinence state makes a difference only at the first three puffs. In summary, for the first three puffs people give higher liking ratings when they are abstinent (vs. non-abstinent).

SPECIFIC AIM 2

Hypothesis 2.1: The correlation for each puff liking rating in the two sessions pre-quit (abstinent and non abstinent) and FTND scores was assessed (Table 3). Analysis revealed that the association between FTND scores and puff liking was generally positive and of small-to-moderate magnitude. In the non-abstinent condition ($n=227$), Pearson's r ranged from .10 to .22, and was significant for five of the seven puffs. In the abstinent condition ($n=215$), Pearson's r ranged from .09 to .19, and was also significant for five of the seven puffs. The magnitude of the correlations appeared broadly similar across puffs and abstinence state. This result was confirmed by entering FTND into a general linear model: There were no significant FTND by

Puff Number ($p=.51$) or FTND by Abstinence State ($p=.34$) interactions, indicating that the effect of FTND on liking did not differ significantly across puffs or abstinence state. In addition, participants who had higher scores on the FTND reported generally higher mean puff liking ratings (Table 3). The associations were of small-to-moderate magnitude, and were of similar magnitude across the two states (Non-abstinent: $r = .19$ and Abstinent: $r = .16$).

Hypotheses 2.2: Mixed ANCOVA and logistic regression were used to assess if participants who have greater hedonic effects from smoking were more likely to relapse to Week +1. (As noted in the Methods chapter, “relapse” was defined as “any smoking, even a puff, during the past 7 days.” Relapse status was verified using self-report, expired breath CO, and cotinine. (Specific cut-off points are included in the Methods chapter.) Overall, Table 2 (right side) and Figure 4 indicated that (subsequent) relapsers appeared to report higher liking ratings (Figure 4). The ANCOVA showed a main effect of Relapse Status, $F(1, 188) = 5.51, p = .02$. There was no Relapse Status by Puff Number interaction or Relapse Status by Abstinence State interaction. As noted earlier, FTND and Order were included as covariates.

When Week +4 was the independent variable, the main effect of Relapse Status was not significant ($p = .17$). Week +4 data are presented to give a comprehensive account of the associations between liking and relapse status.

Logistic regression was also used to examine the association between mean ratings and relapse status at Week +1. Logistic regression revealed a significant relationship between mean puff ratings and relapse at Week 1, $B = 0.37, SE = 0.15, OR = 1.45, 95\% CIs = 1.07 - 1.97, p = .02$. As a participant’s mean puff-rating increases by 1 unit (from example, from a “5” to a “6”), the odds of relapse at Week +1 increase by forty five percent. Stated another way, the odds of

relapse in a smoker with a mean puff liking rating of 6 is forty-five percent higher than the odds of relapse for smoker with a mean rating of 5.

When Week +4 was the independent variable, the main effect of Relapse Status was not significant ($p = .11$). Week +4 data are presented to give a comprehensive account of the associations between liking and relapse status. Future analyses could combine the two time point variables (Week +1 and Week +4) using a multivariate logistic regression model. (This analysis was beyond the scope of the current study).

SPECIFIC AIM 3

Specific Aim 3 used the retrospective ratings (“Overall, how much did you like the cigarette?”) as the dependent variable. Figure 5 shows a graph with the retrospective ratings included. In both states, the mean retrospective puff liking rating is much lower than the average puff liking rating ($p < .001$) and puff liking ratings for the retrospective liking rating are not higher than the liking rating for the final puff (puff 7) in either the non-abstinent ($p = .16$) or abstinent condition ($p = .07$). Therefore, retrospective liking ratings are lower than the mean liking rating and comparable to the liking rating from the final puff, a finding that is consistent with the peak-end rule as described by Kahneman (20).

Hypothesis 3.1: To assess the peak-end rule more formally, a series of regression analyses were performed as described earlier. The dependent variable was the retrospective liking rating. The predictors were peak liking ratings (the highest liking rating recorded), end liking ratings (liking of last puff), and a liking rating from a random puff. Averaged over 20 regressions, Figure 6 shows that the mean coefficients for the peak and the end puff are higher

than the mean coefficient for a random puff for both the non-abstinent and abstinent states (Figure 6).

Hypothesis 3.2: Figure 7 reveals a different pattern than when FTND score was the dependent variable. The peak puff rating is robust predictor of FTND scores (when controlling for the random rating and end rating). However, end puff did not have a positive coefficient suggesting that end puff is not a robust predictor of FTND score.

CHAPTER 5: Discussion

The overall purpose of this study was to explore smokers' self-reported subjective ratings of cigarette "liking." Specifically, the study investigated the pattern of smokers' puff-by-puff liking ratings of a cigarette. Further, the relationship between smokers' subjective ratings of cigarette liking, nicotine dependence, and relapse was studied. Finally, the potential of subjective liking ratings to predict remembered versus experienced utility was explored. Participants who wanted to quit smoking attended six lab sessions. During two pre-quit sessions, participants were asked to smoke 7 puffs of one of their preferred brand of cigarettes. After each puff, they were asked to rate how much they liked each puff. They were also asked to rate their overall liking of the cigarette after the seven puffs were completed. Participants attended two post-quit lab sessions at one-week post-quit day and four weeks post-quit day. At these sessions abstinence was measured via self-report, expired breath CO, and cotinine.

The main findings of the study were as follows. First, individuals differed in their liking ratings for puffs of cigarettes, and liking ratings were highest during the first three puffs when abstinent from smoking. Second, individuals who reported higher liking ratings were more dependent and more likely to relapse during the first week of a smoking cessation attempt. Last, there was some evidence that liking ratings from the peak liking rating was more strongly associated with retrospective ratings and dependence than a rating from a puff selected at random. These findings are discussed further below.

Liking ratings declined over puffs, and liking ratings are higher in the abstinent state for the first three puffs. Liking ratings presumably decline due to the short-term tolerance of the effects of nicotine. This acute tolerance to nicotine is a key feature to understanding the pattern of smoking behavior (31). In their study, Perkins and colleagues reported that after a dosed

treatment of nicotine, participants developed an acute tolerance to several of the subjective effects measured in the study including dose strength, head rush, and tension. The same mechanism may underlie the higher ratings in the abstinent state. Stated briefly, acute hedonic effects may be more potent when nicotinic receptors are less “occupied” by nicotine. However, other variables may be important. For example, we did not measure the dose of nicotine from each puff and it is possible that between-puff differences in liking reflect between-puff differences in nicotine dose. In addition, smoking presumably ameliorates withdrawal symptoms, and this amelioration may be partly responsible for the elevated liking ratings on the first three puffs in the abstinent state.

Participants who get greater hedonic effects from smoking have higher nicotine dependence as measured by FTND scores. Confidence in this finding is bolstered by the fact that it was found in both abstinence states, and by the fact that similar findings were reported by Perkins et al. (28). On the other hand, Shiffman and Kirchner (39) reported no association between subjective satisfaction and nicotine dependence (as measured by the FTND and Nicotine Dependence Syndrome Scale.) Their study used cigarette-by-cigarette satisfaction ratings. Thus, future research is needed to replicate findings using similar measures (all three of these studies used slightly different measures of cigarette liking or satisfaction) to further understand the relationship between smoking liking and dependence.

In addition, participants who got greater hedonic effects from smoking were more likely to relapse to smoking during the first week (controlling for nicotine dependence). These results were similar to findings from Shiffman and Kirchner (39). They stated: “We found that smokers who generally found smoking most satisfying, and particularly most pleasant, were at greater risk for lapsing after they had quit. The effect was not accounted for by nicotine dependence.

This suggests that the memory of how pleasant smoking was may have promoted smoking.” (p.9). Shiffman and Kirchner (39) suggested that the memory of smoking pleasure may be more important to lapsing than the amount of nicotine dependence. The current study found that smokers who reported higher puff ratings were at more risk of early relapse. The study did not examine whether the retrospective liking rating (assessed at the end of the cigarette) was associated with relapse, but this examination could be a priority for future research.

As noted above, the association between liking ratings and relapse were found at Week +1, however, the association between liking ratings and relapse was not significant at Week +4. The meaning of this null effect at Week +4 is not clear and further work should examine whether the magnitude of associations were significantly different for the Week +1 and Week +4 outcomes. Overall, these findings suggest that a lab assessment with only two cigarettes can help identify those at risk for very early relapse (during the first week). For example, in a clinical setting, those smokers with higher puff liking ratings could receive more intensive treatment during the first week of a quit attempt as they may be more likely to relapse during that timeframe. However, additional research is required to determine whether hedonic effects predict relapse status at later time points.

Analyses showed that Peak liking and End (last puff) liking predicted retrospective liking ratings better than liking from a puff selected at random. Interestingly, retrospective liking ratings were well below the average liking rating for the puffs, suggesting that retrospective ratings were biased by the liking rating of the final puff. Peak liking predicted FTND scores better than liking from a puff selected at random in the non-abstinent states. Overall, these results provide some support for the peak end rule. In particular, the peak puff was a good predictor of both retrospective ratings and dependence. This finding suggests that interventions

that specifically reduce peak liking ratings may be effective. For example, a medication could be taken that would reduce the peak puff rating. Initial investigation of galantamine, a drug that inhibits acetylcholinesterase, shows that the drug has the potential to reduce subjective effects of cigarette smoking. Researchers found that galantamine reduced self-reported ratings of craving and liking in a small sample size of smokers (43). Future research would need to explore the outcome of taking a medication such as galantamine on subjective ratings of the peak and end puff rating.

LIMITATIONS

There were several limitations in this study. Self-report measures, used to assess liking and amount smoked, may be subject to response biases (such as social desirability bias). For amount smoked, biochemical confirmation using expired breath CO and cotinine was also used. For liking measures, self-report is the standard method to use in this field of research.

The hedonic effects of smoking in a laboratory setting may not capture the hedonic effects in the participants' natural environment, which limits the external validity of the study. Future studies could employ Ecological Momentary Assessment (EMA) methodology that would ask participants to rate cigarette liking or cigarette puff liking using a Smartphone in their everyday environment.

A third limitation is that the parent study was not designed to address all the specific research questions of this study. If the parent study had been designed to examine experienced and remembered utility, then additional assessments of retrospective ratings could have been added at different time points. For example, instead of using the overall cigarette liking rating measured directly after the seven puffs smoked, an overall liking rating of the cigarette could

have been administered after one hour and after one day. Also, cigarette liking questions could have been included during the one week EMA component of the parent study.

Finally, the results from this analysis are correlational. Therefore, although FTND was controlled for in the relapse analysis, it is possible that a third factor may underlie to association between liking and outcomes.

STRENGTHS

There were several key strengths in this study. First, this is one of the few studies to assess cigarette puff-by-puff liking ratings. Other studies have investigated puff-by-puff smoking topography related to overall liking of a cigarette (28) and cigarette-by-cigarette liking (38). Also, this was the first study to apply the concepts of experienced and remembered utility in smoking research. Given the identified strength of heuristics and biases to sway the way people behave, exploring utility in regards to smoking liking could be a key factor in understanding the complicated mechanisms that power smoking addiction and relapse.

There were also several strengths of the study design. There was a fairly large sample size meaning that the study had power to detect correlations of small-to-moderate magnitude. As mentioned in the limitations section regarding self-report, this study included biochemical validation of abstinence. This measure of abstinence not only allowed for confirmation of relapse status at Week +1 and Week +4, but also allowed for confirmation of abstinence at the abstinent session. This points to another strength of the study design, the inclusion of an abstinent and non-abstinent session. Including these two sessions allowed for exploration of differences of puff liking and overall cigarette liking in two different states.

IMPLICATIONS

The results from this study have several clinical implications. A simple measure of puff liking may be clinically useful to identify individuals at risk of early relapse (in the first week). Individuals identified as being a risk of early relapse could be given additional treatment during the first week of a quit attempt. Also, interventions that attenuate the acute subjective pleasurable effects of smoking may reduce early relapse risk. According to the Odds Ratio, reducing puff rating 1 unit (e.g. from “7” to “6” or from “5” to “4”) may significantly reduce the odds of early relapse by approximately 30%. Recent studies have investigated the effects of medication on subjective effects of acute nicotine and suggest that reductions in hedonic effects may be possible. For example, Sofuoglu et al. (43) reported that the medication galantamine attenuated smokers’ ratings of “good drug effects.” Also, another study used the drug varenicline to assess subjective, physiological, and cognitive measures after nicotine injection. Subjective findings showed an increase in positive mood associated with the medication and a decrease in reported “high” from the nicotine (44). Based on the preliminary findings from this study that decreasing a puff liking rating by one point can significantly reduce the risk of relapse, adding medications that reduce subjective pleasure of smoking (even by one point) could increase the likelihood of a smoker maintaining a quit attempt. Based on the current data, interventions that reduce the peak liking rating may be especially effective.

As described above, medications could potentially be used to reduce the peak liking rating. Another method that should be explored is making smokers aware of the effect of their subjective ratings of “liking,” particularly the peak puff rating. Cessation counselors or psychotherapists could explain the peak-end rule and have smokers conduct their own puff rating or cigarette rating exercise over a week or a day. For some smokers, awareness of the

connection of their own subjective ratings to their ability to quit or dependence ratings may change their subjective ratings of “liking.”

FUTURE DIRECTIONS – RESEARCH IMPLICATIONS

Future studies could build on the findings from this study. Hedonic effects could be assessed both in the lab and in the field (using EMA). As noted earlier, interventions that attenuate the liking effect of smoking could be investigated. These interventions may be especially useful for individuals who experience greater hedonic effects.

Given the preliminary findings regarding utility, future studies could assess relative importance of experienced and remembered utility in dependence. Although remembered utility involved the remembered pleasure of a single cigarette, it could be expanded to cover longer time periods (e.g., remembered pleasure of a week of smoking).

Future analysis should also consider the relationship between nicotine or CO boost from smoking, subjective ratings, and outcomes (such as relapse). CO boost is a measure of smoke exposure that assesses the amount of smoke absorbed by smoking one cigarette (52). Zacny and Stitzer (53) have studied how varying time frames of smoking deprivation affect CO boost (puff volume). Similarly, the relationship between CO boost and subjective ratings of liking could be useful in understanding relapse patterns.

Another aspect that has been researched in this field is the effect of additional contextual variables on cigarette liking. For example, Shiffman and Kirchner (39) discussed the effects of drinking alcohol and smoking around others on self-reported measures of cigarette liking and satisfaction. Future research using EMA methods could assess differences in cigarette liking ratings after/during drinking alcohol, while smoking with others, during stressful periods, etc. to further understand how liking plays a role in the temptation and lapse to smoking.

Finally, an overall goal for additional studies would be to combine measures of *liking* and *wanting* to further understand the psychological underpinnings of smoking relapse. While much research has focused on assessing wanting (craving) of cigarettes, and more research is being conducted on liking/satisfaction of cigarettes, understanding how the two psychological processes work together to influence smoking behavior would assist in understanding the complex mechanisms driving smoking relapse.

Table 1. Participant Demographics and Smoking Characteristics

	M (%)	SD
Sex (% Male)	55.4	
Race (% White)	54.9	
Age in years	43.98	11.79
FTND	5.15	2.02
Time to first cigarette ^a	2.17	0.77
Cigarettes/Day	19.5	8.27
Baseline CO level (ppm)	21.05	10.07
Cotinine levels in saliva (ng/ml) ^d	385.16	223.7
Years smoked	24.15	11.96
Past quit attempts	5.30	3.10
Shipley IQ	104.41	10.78
Education completed in years	14.25	2.2
Annual family income ^{b,c}	5.2	3.36
Site (% USU)	42.0	

Note: Data shown are for the 237 participants who provided puff ratings from at least one smoking assessments. ^aFTND Item 1: Time to the first cigarette of the day (0=after 1hr; 1=31-60mins; 2=6-30mins; 3=within 5mins), ^bIncome before taxes assessed on an 11-pt ordinal scale (4=\$30,000-\$39,999; 5=\$40,000-\$49,999; 6=\$50,000-\$59,999); ^cn=235; ^dn=225 from whom data were available at the non-abstinent session

Table 2. Summary Statistics for Liking Ratings

	All		Week 1 Abstainers		Week 1 Relapsers	
	Non-Abstinent	Abstinent	Non-Abstinent	Abstinent	Non-Abstinent	Abstinent
	n=227	n=215	n=33	n=31	n=166	n=162
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Puff 1	5.46 (1.47)	5.82 (1.46)	5.06 (1.37)	5.55 (1.79)	5.54 (1.48)	5.90 (1.43)
Puff 2	5.37 (1.49)	5.77 (1.43)	4.94 (1.46)	5.52 (1.69)	5.48 (1.44)	5.84 (1.40)
Puff 3	5.22 (1.48)	5.52 (1.50)	4.67 (1.47)	5.03 (1.80)	5.34 (1.47)	5.64 (1.42)
Puff 4	5.02 (1.56)	5.20 (1.59)	4.55 (1.56)	4.61 (1.85)	5.13 (1.55)	5.33 (1.53)
Puff 5	4.81 (1.64)	4.98 (1.58)	4.36 (1.58)	4.39 (1.76)	4.93 (1.64)	5.10 (1.53)
Puff 6	4.72 (1.67)	4.79 (1.66)	4.12 (1.62)	4.32 (1.89)	4.86 (1.67)	4.90 (1.60)
Puff 7	4.58 (1.77)	4.69 (1.76)	3.94 (1.62)	4.16 (1.86)	4.73 (1.77)	4.82 (1.69)
Mean	5.03 (1.43)	5.25 (1.37)	4.52 (1.38)	4.80 (1.58)	5.14 (1.43)	5.36 (1.32)

Note: Mean (SD) for puff liking ratings

Table 3. Correlations between Puff Liking Ratings and FTND scores in the Abstinent and Non-abstinent visits.

	FTND Score	
	Non-Abstinent Visit	Abstinent Visit
Puff 1	.20*	.13
Puff 2	.21*	.14*
Puff 3	.17*	.09
Puff 4	.22*	.16*
Puff 5	.17*	.19*
Puff 6	.12	.14*
Puff 7	.10	.14*
Mean Liking Rating	.19**	.16*

Note: * $p < .05$, ** $p < .01$

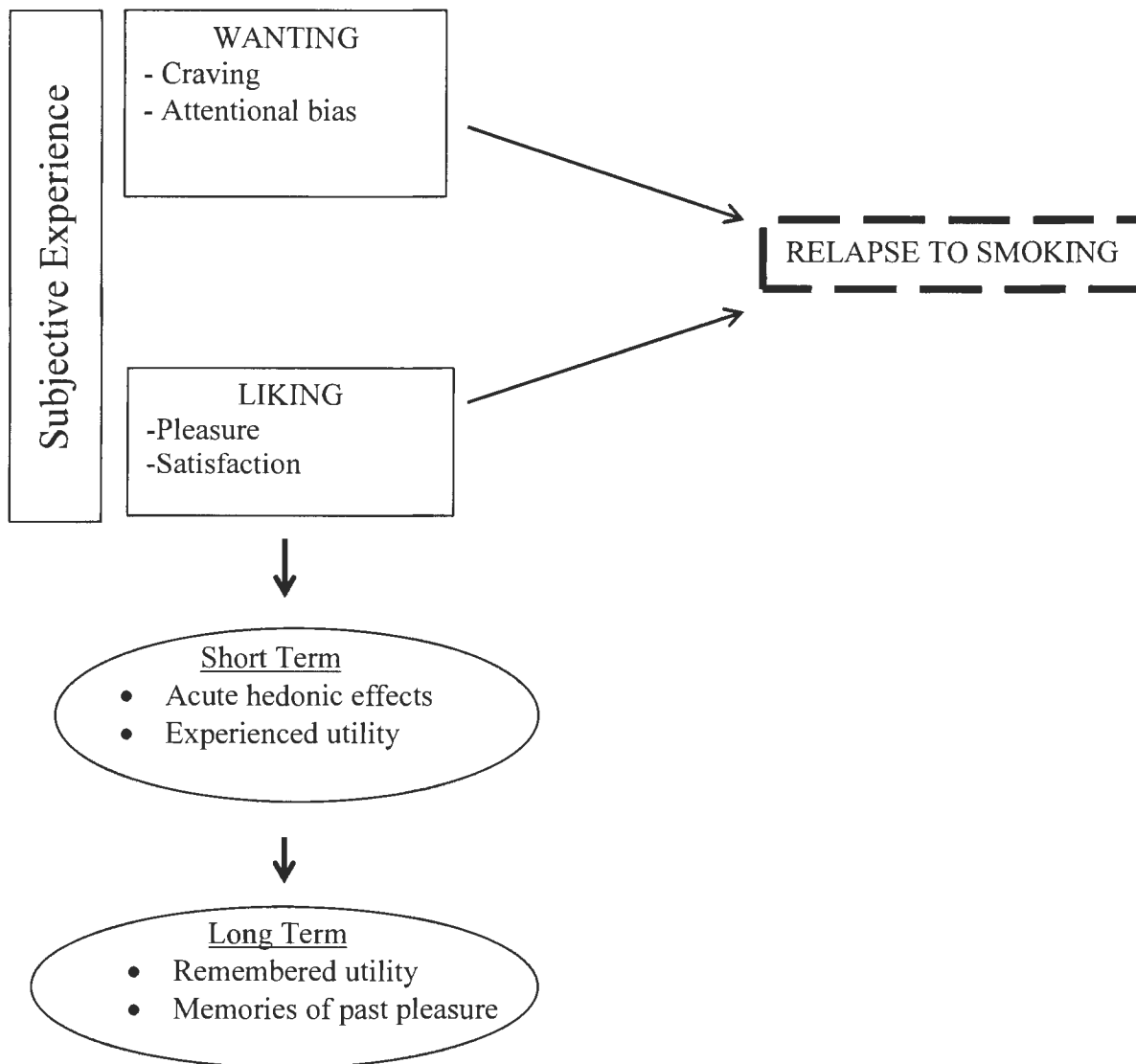


Figure 1. Overall graphic of wanting and liking processes involved in the progression to smoking relapse.

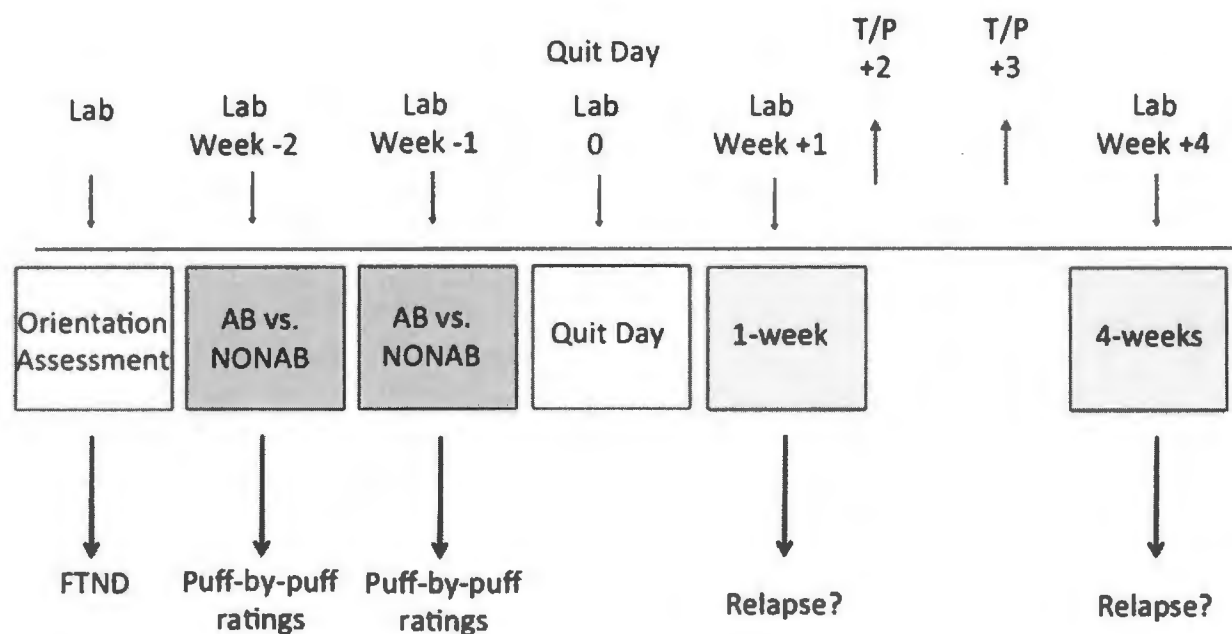


Figure 2. Study design.

Lab = sessions conducted in the laboratory; T/P = counseling sessions conducted via telephone; NON = non-abstinent session (pre-quit); AB = 12 hour abstinent session (pre-quit). Note: Order of completion of NON and AB sessions was counterbalanced across participants.

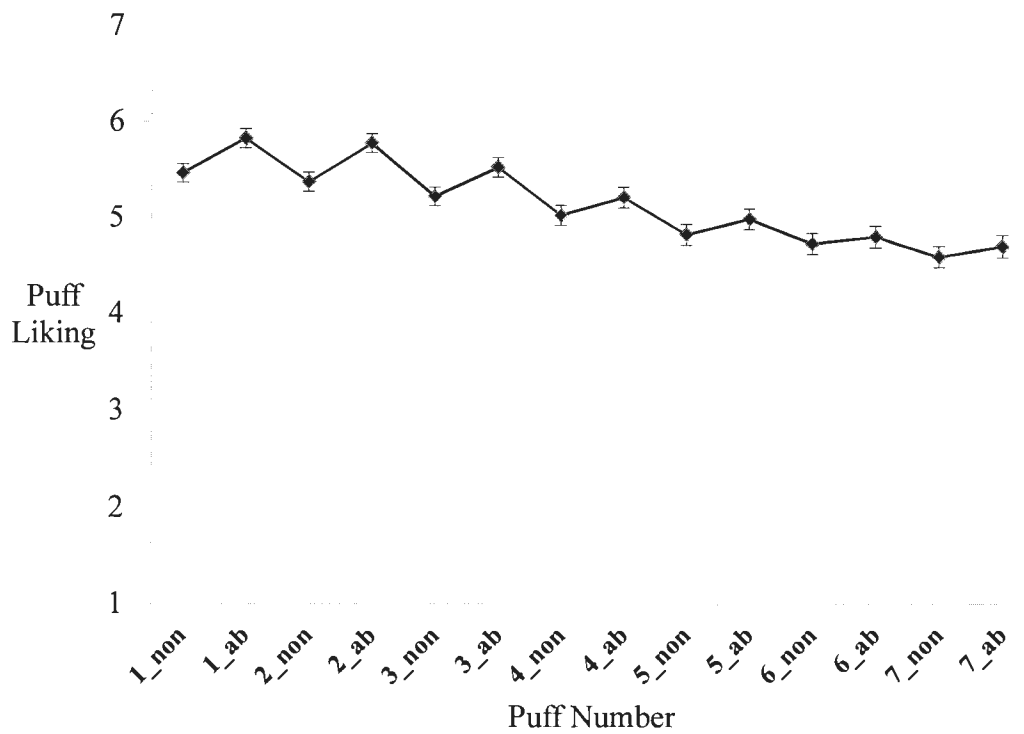


Figure 3. Puff Liking Ratings (1-7 scale) by Puff Number and Abstinence State (N = 227). Data are Mean (± 1 SE). Key: 1_non = puff 1, non-abstinent; 1_ab = puff 1, abstinent, etc.

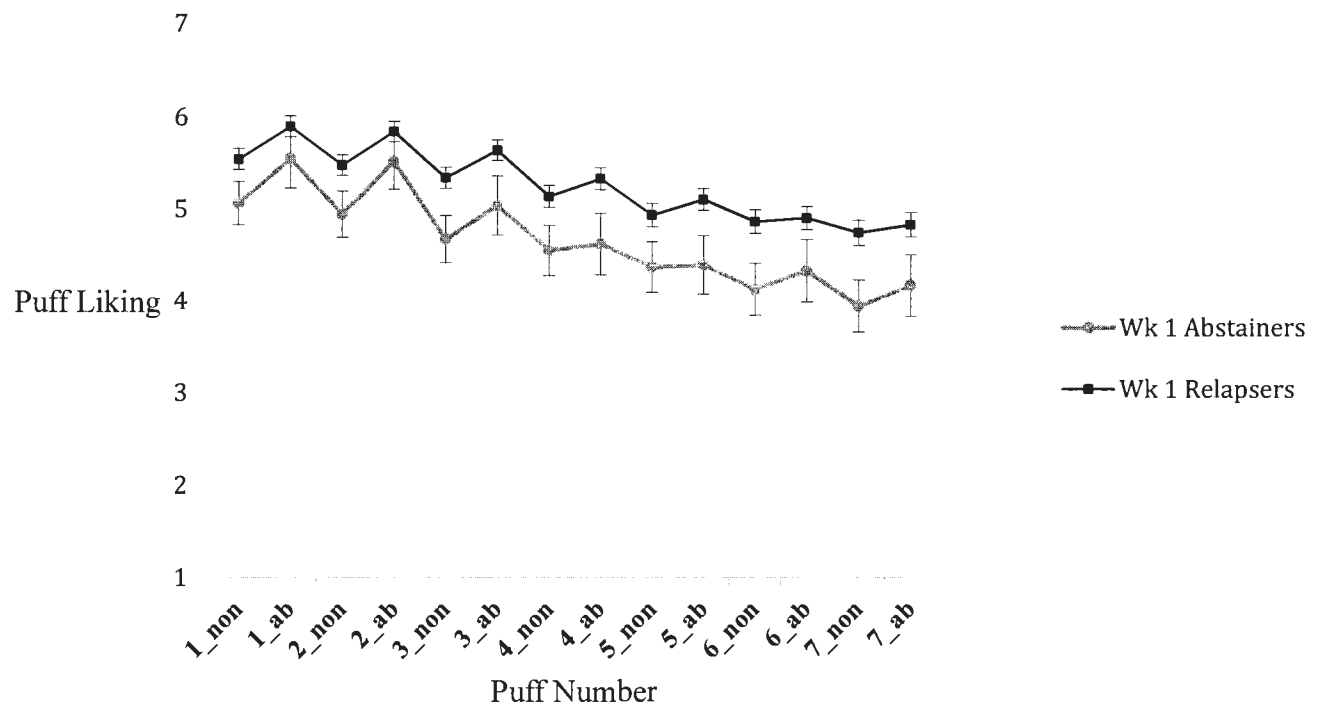


Figure 4. Puff Liking Ratings (1-7 Scale) by Week +1 Relapse status, Puff Number and Abstinence State (ns = 166 relapsers, 33 abstainers (non-abstinent); 162 relapsers, 31 abstainer (abstinent state)).

Data are Mean (± 1 SE). Key: 1_non = puff 1, non abstinent; 1_ab = puff 1, abstinent, etc.

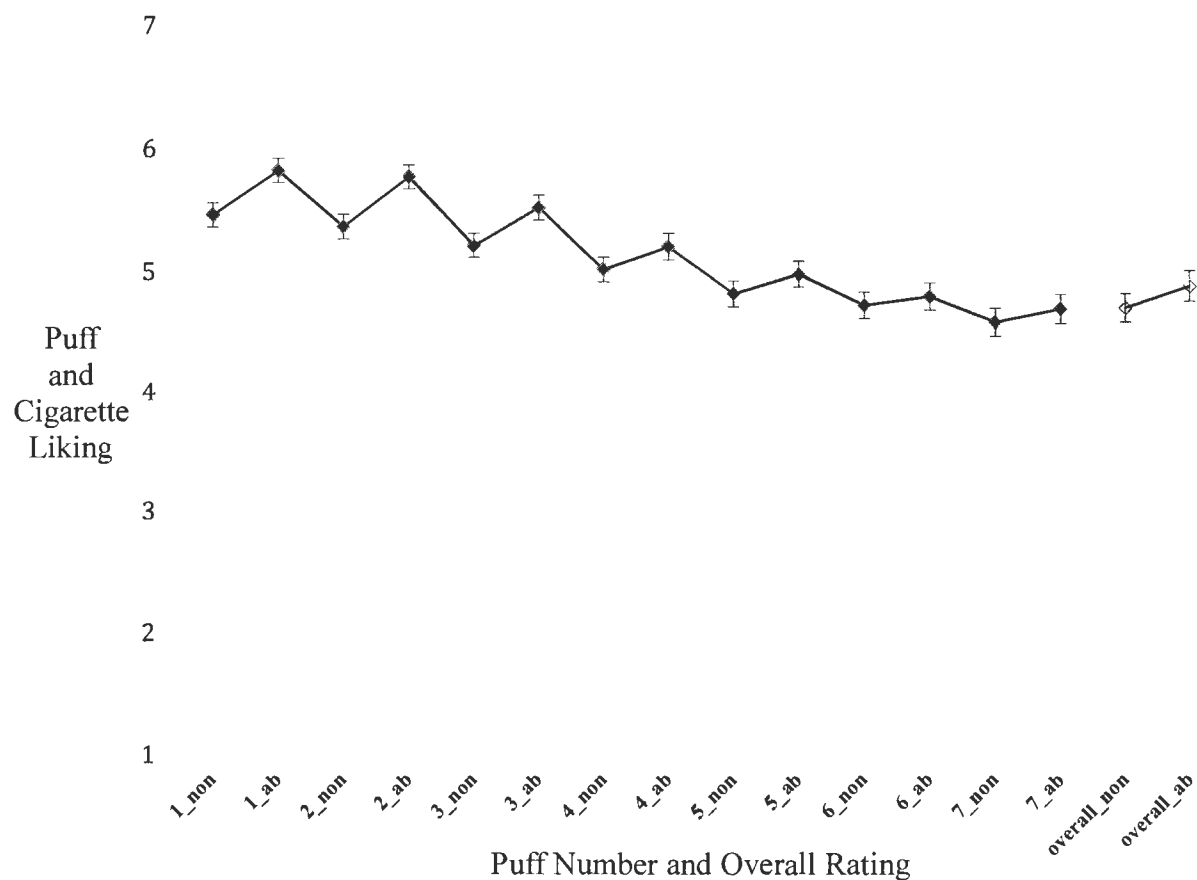


Figure 5. Mean retrospective ratings with Puff Liking Ratings (1-7 scale) by Puff Number and Abstinence State (N = 227).

Data are Mean (± 1 SE). Key: 1_non = puff 1, non-abstinent; 1_ab = puff 1, abstinent, etc.; overall_non = retrospective liking rating in non-abstinent condition, overall_ab = retrospective liking rating in abstinent condition.

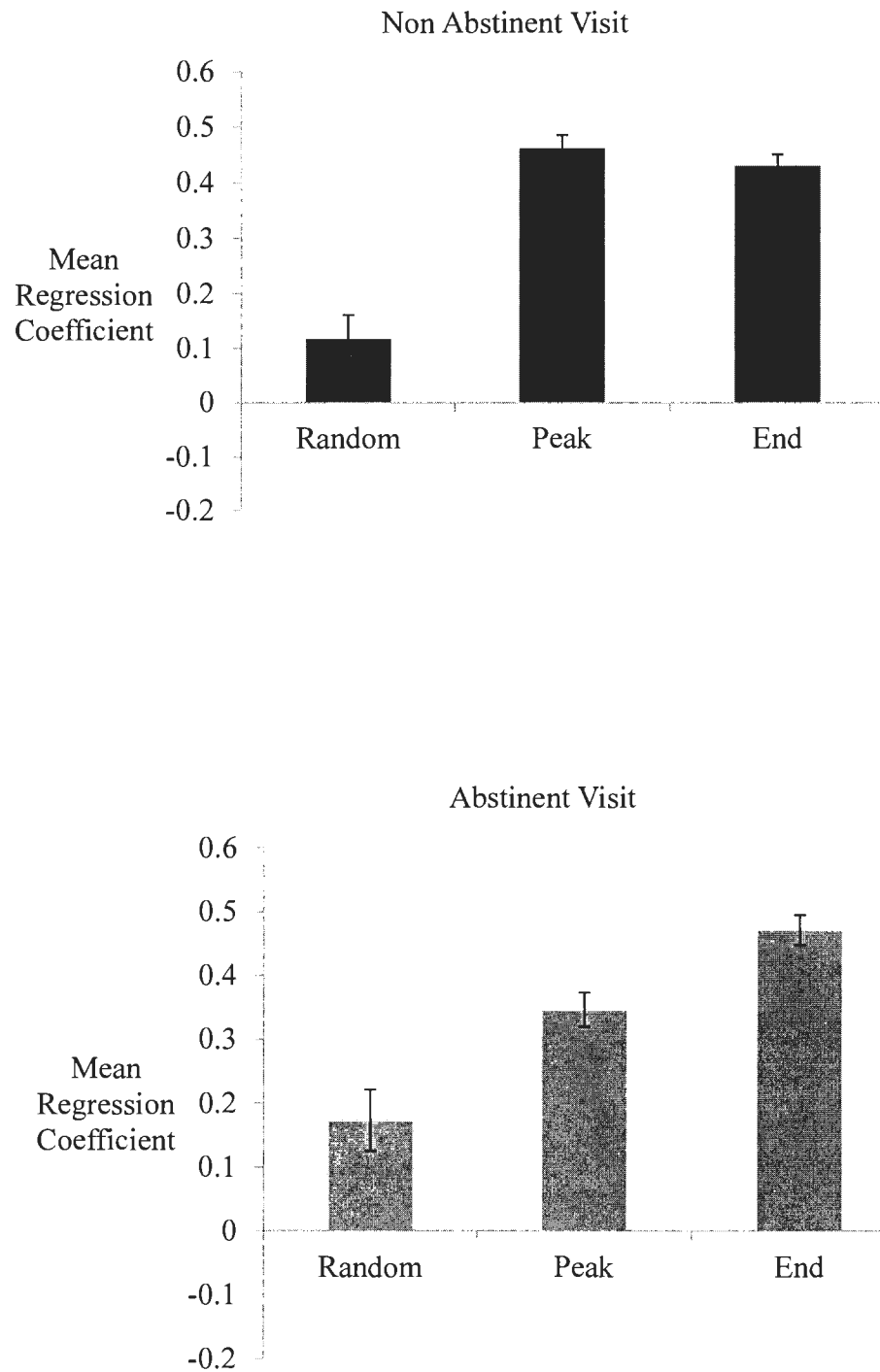


Figure 6. Peak-end analysis for retrospective ratings of cigarette liking. Data are Mean unstandardized regression coefficients (95% Confidence Intervals) aggregated over 20 multiple linear regressions with retrospective liking ratings as the dependent variable and random puff liking, peak puff liking, and end puff liking as independent variables (see text for details).

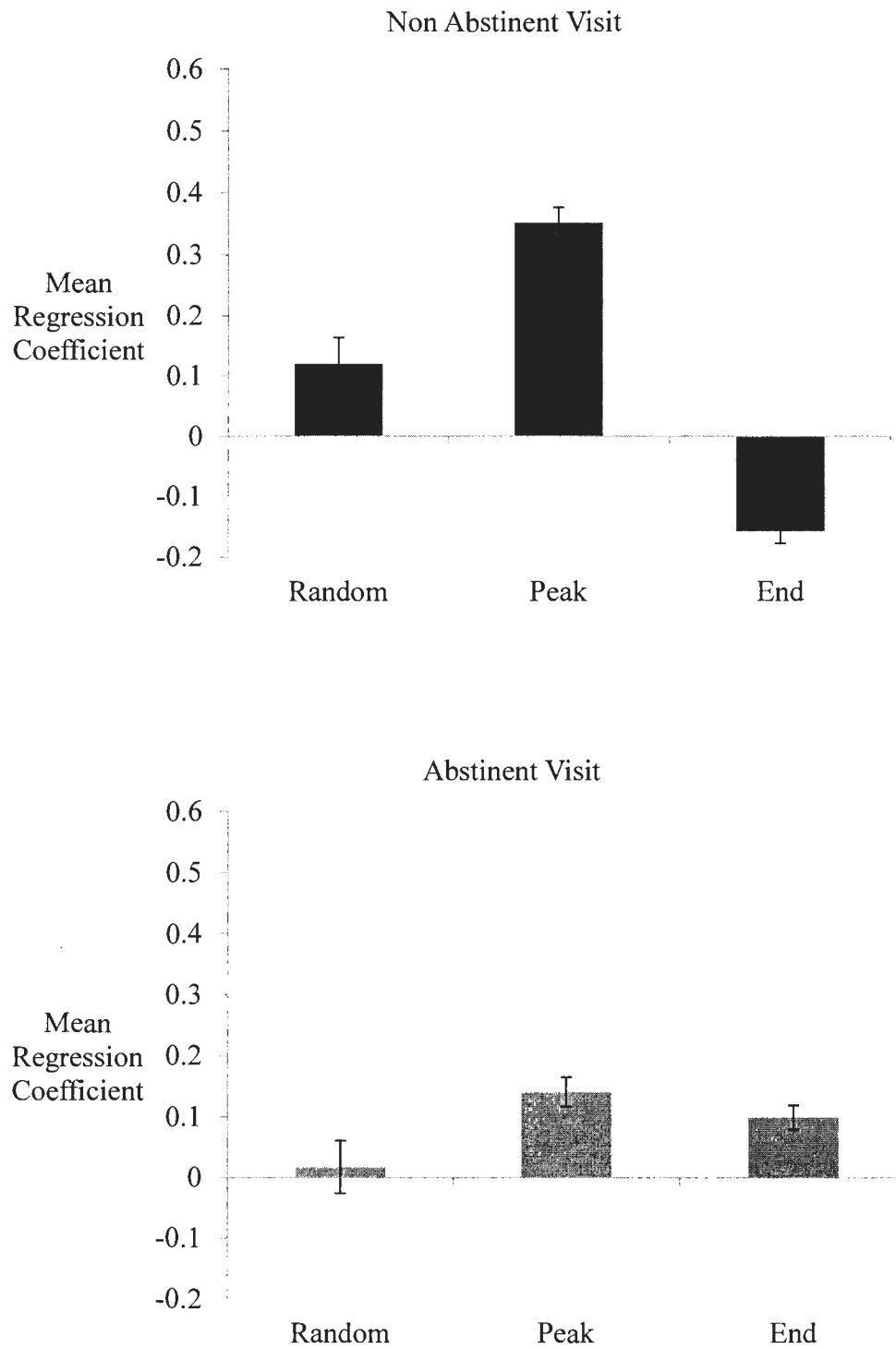


Figure 7. Peak-end analysis for FTND.

Data are Mean unstandardized regression coefficients (95% Confidence Intervals) aggregated over 20 multiple linear regressions with FTND score as the dependent variable and random puff liking, peak puff liking, and end puff liking as independent variables (see text for details).

Appendix A: USUHS IRB Approval



UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799



September 8, 2009

MEMORANDUM FOR DR. ANDREW WATERS, PH.D., MEDICAL AND CLINICAL PSYCHOLOGY

SUBJECT: Uniformed Services University Institutional Review Board (FWA 00001628; DoD Assurance P60001) Approval regarding Human Subjects Research Protocol G172JY

Congratulations! The amendment for your No More Than Minimal Risk human subjects research protocol G172JY, entitled "*Cognitive Processes in Smoking Cessation*," was reviewed and approved for execution on Tuesday, September 8, 2009 by Edmund G. Howe III, M.D., J.D., Chairperson, Uniformed Services University IRB, under the provisions of 32 CFR 219.110(b)(2). This approval will be reported to the full Uniformed Services University IRB scheduled to meet on Thursday, October 15, 2009.

The purpose of this behavioral research study is to find out which types of smokers are in need of more help with quitting smoking.

This action approves amendment #5 that: (1) adds two study personnel (CITI complete 7/18/09 and 8/13/09); (2) revises recruitment numbers up to 250 to account for participants who sign the ICD but are later deemed ineligible; (3) makes minor revisions to the ICD regarding compensation; and (4) adds venues for study advertisements (utilizing the previously approved advertisements).

Authorization to conduct protocol G172JY will automatically terminate on Tuesday, January 5, 2010. You are authorized to enroll up to 250 subjects in this study. If you plan to continue data collection or analysis beyond this date, IRB approval for continuation is required. Please submit a USU Form 3204A/B (application for continuing approval) to the IRB Office 60 days prior to the termination date. The IRB Office will attempt to assist you by sending you a reminder; however, submission of an application for continuation is your responsibility. Please note the termination date and the date for submission of your USU Form 3204A/B in your calendar!

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human research for this project to this office for review. No changes to this protocol may be implemented prior to IRB approval. If you have questions regarding this IRB action, or questions of a more general nature concerning human participation in research, please contact the undersigned at mstretch@usuhs.mil or (301) 295-0819.

Micah Stretch, M.A., J.D.
IRB Coordinator

cc: ☐ Mr. MPM
☐ VPC
☒ File

Appendix B: MDACC Approval of Data Transfer

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Office of Protocol Research

Institutional Review Board (IRB)
Unit 1437
Phone 713-792-2933
Fax 713-794-4589

To: Paul Cinciripini 03/31/2009
From: Marion B. Olson
CC: Sunetra Martinez, Victoria L. Brown, Evanna L. Thompson, Veronica Roberts
MDACC Protocol ID #: 2005-0741
Protocol Title: Cognitive Processes in Smoking Cessation
Version: 13

Subject: Administrative IRB Approval – Protocol 2005-0741

On Tuesday, 03/31/2009, the Institutional Review Board (IRB) 4 chair or designee reviewed and approved your revision dated 03/27/2009 for Protocol 2005-0741

These Pages Include:

Protocol Body – Document header Date: 03/27/2009

Revision included the following changes:

Clarifying that the de-identified data will be sent to Dr. Andrew Waters and his statistical team at the Uniformed Services University of the Health Sciences.

Additional Revision History:

Please note that along with this revision the M. D. Anderson IRB approves the transfer of de-identified study data for analysis to Dr. Andrew Waters, collaborator on this study, and his statistical team at the Uniformed Services University of the Health Sciences.

The revision can now be implemented. Please inform the appropriate individuals in your department or section and the collaborators of these changes.

Please inform the appropriate individuals in your department/section and your collaborators of these revisions.

Please Note: This approval does not alter or otherwise change the continuing review date of this protocol.

In the event of any questions or concerns, please contact the sender of this message at (713) 792-2933.

Marion B. Olson 03/31/2009 10:02:17 AM

This is a representation of an electronic record that was signed electronically and below is the manifestation of that electronic signature:

Marion B. Olson
03/31/2009 09:51:14 AM

IRB 4 Chair Designee
FWA #: IRB00005015

Appendix C: USUHS Informed Consent Form

This consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Non-Clinical Research Study

1. INTRODUCTION OF THE STUDY

You are being asked to be in a research study entitled, “Cognitive Processes in Smoking Cessation”, at the Uniformed Services University (USU), Bethesda, Maryland. You have been asked to take part in this study because you are a smoker, and you want to quit smoking. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in the study.

2. PURPOSE OF THE STUDY

The purpose of this behavioral research study is to find out which type of smokers are in need of more help with quitting smoking. This study may help researchers create more effective cessation (quitting) programs. Researchers want to learn the reasons why some smokers who quit smoking choose to start up again (relapse) more quickly than other smokers. Also, researchers want to use computerized tasks to help predict who is likely to relapse.

Other studies have shown that some computerized tasks are helpful in determining which smokers are likely to relapse more quickly. We want to carry out more research using additional tests.

3. PROCEDURES TO BE FOLLOWED

If you agree to be in this study, you will be asked to attend a total of 6 sessions at USU. At the first session (orientation), you will complete a breath test that allows the investigators to know how much you smoke. You will also complete about 7 questionnaires, which will take a total of about 1 hour to complete. The questionnaires will ask about you and your health, your smoking habits, and your drinking habits. There will also be a brief reading test, which will take about 5 minutes to complete. It will check your reading ability. The orientation will help researchers learn if you are eligible to participate in this study.

If you are found to be eligible and you wish to take part in this study, you will attend 5 laboratory sessions at USU. You will attend 2 sessions before trying to quit, 1 session on your quit day, 1 session one week after your quit day, and a final session 1 month after your quit day. At each of these laboratory sessions, you will complete a series of computerized evaluations, which will take about 90 minutes to complete. These evaluations are reaction-time tests.

At the 2 pre-quit sessions, you will be asked to smoke a cigarette (after the computerized evaluation). Before one of these pre-quit sessions, which will be picked randomly, you will be asked to stop smoking for 12 hours before the session.

During each of the laboratory sessions, you will also complete about 7 questionnaires that ask about your mood, cigarette cravings, and smoking habits. These questionnaires will take about 30 minutes in total to complete at each session. You will also be asked to complete a breath test and to provide a saliva sample. The breath test and the saliva sample will help the researchers find out how much you have smoked.

You will also be called on 2 occasions after your quit day, and you will be asked some questions about your smoking. Each phone call will last about 15 minutes. During the study, a staff member will meet with you for 10 to 20 minutes and help you to try and quit. You will meet with the staff member at each of the laboratory sessions. Every participant will receive the same help.

Some participants will be asked to carry a handheld computer (PDA) around for 1 week after their quit day. The PDA will beep randomly about 4 times a day (random assessments). Participants will answer some questions about their mood and craving, and complete a computerized reaction time task. Each assessment takes about 5 minutes.

Participation in this study will be over after your final visit to USU, which will be 4 weeks after your quit day.

4. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

Up to 250 subjects are expected to take part in this study at USU.

5. AMOUNT OF TIME FOR YOU TO COMPLETE THE STUDY

If you are eligible, you will be part of this study for about 7 weeks.

ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

Civilians and military personnel may be paid for participation in this study. Payments will be made after each visit, as described above.

Civilians (non-federal). You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete, and you will receive this at the final laboratory session. Participants who carry around the PDA for a week will receive \$2.50 for each random assessment that they complete.

Civilians (federal). You will only receive compensation for laboratory sessions/telephone assessments if those sessions occur during non-duty hours. In addition, if you wish to be

compensated for participation during non-duty hours, you must file a request for outside activity. If

the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Federal civilians may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Uniformed Personnel. You will only receive compensation for laboratory sessions if those sessions occur during non-duty hours. In addition, if you wish to be compensated for participation during non-duty hours, you must file a request for outside activity. If the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Uniformed personnel may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Please Note: Federal Civilians and Uniformed Personnel should inform their supervisors about the study for which they are volunteering whether or not they will receive compensation.

At the orientation session, if you are ineligible for the study because the breath test indicates that you have low levels of carbon monoxide in your breath, the orientation session will end right away and you will receive \$10 for your time and travel expenses. If you are ineligible for another reason, the session will last for a longer duration and you will receive \$25 for your time and travel expenses. Payments to ineligible participants follow the same rules as those written above for the eligible participants.

7. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

The expected risks or discomforts from being in this study are expected to be minimal. There are no known risks associated with the computerized evaluations. On 1 pre-quit session, you will arrive having not smoked on that day. You may experience symptoms of nicotine withdrawal, which include restlessness, difficulty concentrating, and/or mood changes. You will also smoke a cigarette at each of the pre-quit visits. Though smoking is considered bad for your health, your smoke intake is not likely to be increased by participating in this study. (Your smoke intake is likely to be decreased by participating in the study).

You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaires, you are encouraged to contact your doctor or the study chair.

If something in this research makes you uncomfortable or upset, you may choose to stop taking part in this research at any time without loss of benefits; you may contact the investigator for referral. If the investigators note any distress or anxiety associated with the research, you will receive referrals, if appropriate.

POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You may benefit from this study because if you are able to quit, this may be very beneficial to your health. Future smokers may benefit from what is learned. The information we learn may help us learn to develop better smoking cessation programs.

However, no benefit can be guaranteed.

9. CONFIDENTIALITY/PRIVACY AND HOW YOUR IDENTITY AND YOUR RESEARCH RECORDS WILL BE MAINTAINED

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Your responses to our interviews and questionnaires, as well as audio-taped sessions will be maintained in a locked filing cabinet in lab offices in the Department of Medical and Clinical Psychology. All records related to this study will be accessible to those persons directly involved in conducting this study and members of the USUHS Institutional Review Board (IRB), which provide oversight for protection of human research volunteers. In addition, the IRB at USUHS and other federal agencies that help protect people who are involved in research studies, may need to see the information you give us. Other than those groups, records from this study will be kept private to the fullest extent of the law. Scientific reports that come out of this study may include your ideas, but they will not use your name or identify you in any way.

10. CONDITIONS WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

The investigator may stop you from taking part in this study if being in the study is unsafe or dangerous to you or if you lose your right to receive medical care at military hospitals. The investigator may also stop you participating if you experience difficulty in following the procedures.

11. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND THE INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible; by leaving this study at any time, you in no way risk losing your right to medical care.

12. RECOURSE IN THE EVENT OF INJURY

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Director of Human Research Protections Program at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-9534. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

CONTACT FOR QUESTIONS OR PROBLEMS

If you have questions about this research, you should contact Andrew J. Waters, Ph.D. the person in charge of the study. His phone number at USUHS is 301 295-9675. Even in the evening or on weekends, you can leave a message at that number. If you have questions about your rights as a research subject, you should call the Director of Human Research Protections Program at USUHS at (301) 295-9534. She is your representative and has no connection to the researcher conducting this study.

SIGNATURE OF RESEARCH PARTICIPANT OR LEGAL REPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Participant's Signature

Date

Participant's Printed Name

SIGNATURE OF INVESTIGATOR/RESEARCH TEAM MEMBER

You have explained the research to the participant, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's/Research Team Member's Signature Date (must be the same as the participant's)

Investigator's/Research Team Member's Printed Name

SIGNATURE OF WITNESS

Your signature as witness is intended to attest that the information in the consent document and any other information was explained to and apparently understood by the participant, or the participant's legal representative, that questions and concerns were addressed and that informed consent was freely given.

Witness' Signature

Date (must be the same as the participant's)

Witness' Printed Name

Appendix D: CO Monitor Instructions

Micro Operating Manual

English

Quick Start Guide

- 1 Press the on/off button until the display becomes active. Release the button.
- 2 Insert the D-piece into the instrument and a new Steribreath™ mouthpiece.
- 3 Touch the  icon to start a breath test. 
- 4 This starts the breath-hold countdown. The patient should inhale deeply and hold their breath while the display counts down to zero. If unable to hold their breath for the full countdown, see Warnings on page 4 or Settings on page 12. 
- 5 The  bleep will sound during the last three seconds of the countdown.
- 6 At end of the countdown, the patient should blow slowly into the mouthpiece, and exhale until their lungs are empty. 
- 7 The ppm and %COHb value will rise, and the highest level will hold. 
- 8 To view the corresponding %FCOHb, touch the . 
- 9 Remove and dispose of the Steribreath™ mouthpieces.
- 10 Remove the D-piece between tests to allow fresh air to purge sensor.
- 11 Touch  to perform another breath test. A new mouthpiece is required.
- 12 To switch off, press the on/off button for 3 seconds. Unit will also auto power-off after 5 minutes of inactivity.



APPENDIX E: Self-Report Measures

FAGERSTRÖM TEST FOR NICOTINE DEPENDENCE

	Within 5 minutes	6 to 30 minutes	31 to 60 minutes	After 60 minutes
1. How soon after you wake up do you smoke your <u>first</u> cigarette?			Yes	No
2. Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in the cinema, etc.?			1st one in the A.M.	All others
3. Which cigarette would you hate to give up most?				
	10 or less	11-20	21-30	31 or more
4. How many cigarettes per day do you smoke?				
			Yes	No
4. Do you smoke more frequently during the first hours after waking than the rest of the day?				
			Yes	No
5. Do you smoke if you are so ill that you are in bed most of the day?				

PUFF-BY-PUFF RATINGS

How much did you like the last puff?						
1	2	3	4	5	6	7
Didn't like it at all						Liked it very much

OVERALL CIGARETTE RATINGS

Cigarette Ratings

Overall, how satisfying did you find the cigarette?

1	2	3	4	5	6	7
Not satisfying at all						Extremel y satisfying

Overall, how much did you like the cigarette?

1	2	3	4	5	6	7
Didn't like it at all						Liked it very much

Overall, how much did you enjoy the cigarette?

1	2	3	4	5	6	7
Didn't enjoy it at all						Extremel y enjoyable

SMOKING DIARY

Study ID: _____

Tobacco Use Record Form

Instructions for Participant:

- Complete this form each day.
- Just before going to sleep, indicate how many cigarettes you have smoked that day.
- Be honest... Accurate information is important!

I agree to complete this form every night. I will provide information that is as accurate as possible.

SIGNATURE AND DATE:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1							
Week 2							
Week 3							

REFERENCES

1. Berridge KC. 2007. The debate over dopamine's role in reward: the case for incentive salience. *Psychopharmacology*. 191:391-431
2. Berridge KC, Robinson TE. 1998. What is the role of dopamine in reward: Hedonic impact, reward learning, or incentive salience? *Brain. Res. Rev.* 28:309-69
3. Brewer JA, Mallik S, Babuscio TA, Nich C, Johnson HE et al. 2011. Mindfulness Training for smoking cessation: results from a randomized controlled trial. *Drug Alcohol Depen.* 119:72-80
4. Brown DW. 2010. Smoking prevalence among US Veterans. *J. Intern. Med.* 25: 147-49
5. Brown RA, Burgess ES, Sales SD, Whiteley JA, Evans DM, Miller IW. 1998. Reliability and validity of a smoking timeline follow-back interview. *Psychol. Addict. Behav.* 12:101-12
6. Centers for Disease Control and Prevention. 2014. Current cigarette smoking among adults – United States, 2005 – 2012. *Morbidity and Mortality Weekly Report*. 63:29-34
7. Centers for Disease Control and Prevention. 2011. Current cigarette smoking prevalence among working adults – United States, 2004 – 2010. *Morbidity and Mortality Weekly Report*. 60:1305–09
8. Chapman M, MacKenzie R. 2010. The global research neglect of unassisted smoking cessation: Causes and consequences. *PLoS Med.* 7:2
9. Cinciripini PM, Robinson JD, Carter BL, Lam C, Wu X, deMoor CA, Baile WF, Wetter DW. 2006. The effects of smoking deprivation and nicotine administration on emotional reactivity. *Nicotine Tob. Res.* 8:379-92
10. Davis TC, Long SW, Jackson RH, Mayeaux EJ, George RB, Murphy PW, Crouch MA. 1993. Rapid estimate of adult literacy in medicine: a shortened screening instrument. *Fam. Med.* 25:391-95
11. Department of Defense. 2013. *2011 DoD Survey of Health Related Behaviors Among Active Duty Military Personnel*. Washington D.C.: Department of Defense
12. Ferguson SG, Shiffman S. 2014. Effect of high dose nicotine patch on craving and negative affect leading up to lapse episodes. *Psychopharmacology*. 23:2595-602
13. Gifford EV, Kohlenberg BS, Hayes SC, Pierson HM, Piasecki MP, Antonuccio DO, Palm KM. 2011. Does acceptance and relationship focused behavior therapy contribute to bupropion outcomes? *Behav. Ther.* 42:700-15

14. Gorber SC, Schofield-Hurwitz S, Hardt J, Levasseur G, Tremblay M. 2009. The accuracy of self-reported smoking: A systematic review of the relationship between self-reported and cotinine-assessed smoking status. *Nicotine Tob. Res.* 11:12-24
15. Hajek P, Stead LF, West R, Jarvis M, Lancaster T. 2009. Relapse prevention interventions for smoking cessation. *Cochrane Database Syst. Rev.* 2013:8
16. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. 1991. The Fagerstrom Test for Nicotine Addiction: A revision of the Fagerström Tolerance Questionnaire. *Brit. J. Addict.* 86:1119-27
17. Goldberg SR, Speelman RD, Risner ME, Henningfield JE .1983. Control of behavior by intravenous nicotine injections in human subjects. *Pharmacol. Biochem. Behav.* 19:1011-20
18. Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. 2014. Antidepressants for Smoking Cessation (Review), *Cochrane Database Syst. Rev.* 2014:1
19. Institutes of Medicine. 2009. *Combating tobacco in military and veteran populations*. Washington, DC: Institutes of Medicine.
http://books.nap.edu/openbook.php?record_id=12632
20. Kahneman D. 2000. Evaluation by moments: Past and future. In *Choices, Values, and Frames*, ed. D Kahneman, A Tversky, pp. 693-708. New York: Cambridge University Press
21. Kalman D. 2002. The subjective effects of nicotine: Methodological issues, a review of experimental studies and recommendations for future research. *Nicotine Tob. Res.* 4:25-70
22. Kozlowski LT, Wilkinson DA. 1987. Use and misuse of the concept of craving by alcohol, tobacco, and drug researchers. *Brit. J. Addict.* 82:31-36
23. Kroenke K, Spitzer RL, Williams JBW. 2001. The PHQ-9 validity of a brief depression severity measure. *J. Gen. Intern. Med.* 16:606-13
24. Leidner AJ, Shaw WD, Yen ST. 2014. An historical perspective on health-risk awareness and unhealthy behavior: Cigarette smoking in the United States 1949-1981. *Health Expectations*. doi: 10.1111/hex.12246
25. Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lingren L, et al. 2014. Smoking prevalence and cigarette consumption in 187 countries, 1980-2012. *J. Am. Med. Assoc.* 311:183-92
26. Nixon SJ, Parsons OA, Schaeffer KW, Hale RL. 1995. A methodological study of the Shipley Institute of Living Scale in alcoholics and non-alcoholics: reliability, discriminating items and alternate forms. *Appl. Neuropsych.* 2:155-60
27. Ossip-Klein DJ, Bigelow G, Parker SR, Curry S, Hall S, Kirkland S. 1986. Task force 1: Classification and assessment of smoking behavior. *Health Psychol.* 5:3-11

28. Perkins KA, Karelitz JL, Giedgowd GE, Conklin CA. 2012. The reliability of puff topography and subjective responses during ad lib smoking of a single cigarette. *Nicotine Tob. Res.* 14:490-94
29. Perkins KA, Lerman C, Grottenthaler A, Ciccocioppo MM, Milanak ME, et al. 2008. Dopamine and Opioid gene variants are associated with increased smoking reward and reinforcement due to negative mood. *Behav. Pharmacol.* 19:641-49
30. Perkins KA, Grobe JE, Mitchell SL, Goettler J, Caggiula A, Stiller RL, Scierka A. 1995. Acute tolerance to nicotine in smokers: Lack of dissipation within 2 hours. *Psychopharmacology.* 118:164-70
31. Perkins KA, Grobe JE, Fonte C, Goettler J, Caggiula A, et al. 1994. Chronic and acute tolerance to subjective, behavioral and cardiovascular effects of nicotine in humans. *J. Pharmacol.* 270:628-38
32. Pomerleau CS, Carton SM, Lutzke ML, Flessland KA, Pomerleau OF. 1994. Reliability of the Fagerström Tolerance Questionnaire and Fagerström Test for Nicotine Dependence. *Addict. Behav.* 19:33-39
33. Pomerleau CS, Pomerleau OF. 1992. Euphoriant effects of nicotine in smokers, *Psychopharmacology.* 108:460-65
34. Robinson TE, Berridge KC. 1993. The neural basis of drug craving: an incentive-sensitization theory of addiction. *Brain Res. Rev.* 18:247-91
35. Sheehan DV, Lecrubier Y, Harnett Sheehan K, Janavs J, Weiller E, et al. 1997. The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. *Eur. Psychiat.* 12:232-41
36. Shiffman S, Engberg JB, Paty JA, Perz WG, Gnys M, Kassel JD, Hickcox M. 1997. A day at a time: Predicted smoking lapse from daily urge. *J. Abnorm. Psychol.* 106: 104-16
37. Shiffman S, Ferguson SG, Gwaltney CJ. 2006. Immediate hedonic response to smoking lapses: Relationship to smoking relapse, and effects of nicotine replacement therapy. *Psychopharmacology.* 184:608-18
38. Shiffman S, Gwaltney CJ, Balabanis MH, Liu KS, Paty JA, et al. 2002. Immediate antecedents of cigarette smoking: An analysis from ecological momentary assessment. *J. Abnorm. Psychol.* 111:531-45
39. Shiffman S, Kirchner TR. 2009. Cigarette-by-cigarette satisfaction during ad libitum smoking. *J. Abnorm. Psychol.* 118:348-59
40. Shiffman S, Waters AJ. 2004. Negative affect and smoking lapses: A prospective analysis. *J. Consult. Clin. Psych.* 72:192-201

41. Silagy C, Lancaster T, Stead L, Mant D, Fowler G. 2004. Nicotine replacement therapy for smoking cessation (review). *Cochrane Database Syst. Rev.* 2004:3
42. Silverstein P. 1992. Smoking and wound healing. *Am J. Med.* 93: S22-S24
43. Sofuoglu M, Herman AI, Li Y, Waters AJ. 2012. Galantamine attenuates some of the subjective effects of intravenous nicotine and improves performance on a Go No-Go task in abstinent cigarette smokers: a preliminary report. *Psychopharmacology.* 224:413-20
44. Sofuoglu M, Herman AI, Mooney M, Waters AJ. 2009. Varenicline attenuates some of the subjective and physiological effects of intravenous nicotine in humans. *Psychopharmacology.* 207:153-62
45. SRNT Subcommittee on Biochemical Verification. 2002. Biochemical verification of tobacco use and cessation. *Nicotine Tob. Res.* 4:149-59
46. Stefano GB, Bianchi E, Guarna M, Fricchione GL, Zhu W, et al. 2007. Nicotine, alcohol and cocaine coupling to reward processes via endogenous morphine signaling: The dopamine-morphine hypothesis. *Med. Sci. Mon.* 13:91-102
47. U.S. Dept of Health and Human Services .1988. *The health consequences of smoking: Nicotine addiction. A Report of the Surgeon General.* Washington, DC: U.S. Government Printing Office. <http://profiles.nlm.nih.gov/NN/B/B/Z/D/>
48. U.S. Dept of Health and Human Services. 2014. *The health consequences of smoking – 50 years of progress: A report of the Surgeon General.* Washington, DC: U.S. Government Printing Office. <http://www.surgeongeneral.gov/library/reports/50-years-of-progress/index.html>
49. Waters AJ, Szeto EH, Wetter DW, Cinciripini PM, Robinson JD, Li Y. 2014. Cognition and craving during smoking cessation: An Ecological Momentary Assessment Study. *Nicotine Tob. Res.* 16:111-18
50. Wong M, Krajisnik A, Truong L, Lisha NE, Trujillo M, et al. 2012. Anxiety sensitivity as a predictor of acute subjective effects of smoking. *Nicotine Tob. Res.* 15:1084-90
51. Yeomans K, Payne KA, Marton JP, Merikle EP, Proskorovsky I, et al. 2011. Smoking, smoking cessation and smoking relapse patterns: a web-based survey of current and former smokers in the US. *Int. J. Clin. Prac.* 65:1043-54
52. Zacny JP, Stitzer ML. 1994. Human Smoking Patterns. In *The FTC Cigarette Test Method for Determining Tar, Nicotine, and Carbon Monoxide Yields of U.S. Cigarettes*, ed. DR Shopland, pp. 151-60. Bethesda, National Cancer Institute
53. Zacny JP, Stitzer ML. (1985). Effects of smoke deprivation interval on puff topography. *Clin. Pharm. Ther.* 38:109-15